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ENDOMETRIAL HYPERPLASIA AND CARCINOMA OF THE BODY OF THE UTERUS*

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ETIOLOGIC studies upon the glandular carcinomas of the body of the uterus have been few in comparison with the immense amount of work devoted to the cancer arising from the squamous epithelium of the cervix. As a result of the attention devoted to the latter, a group of lesions exhibiting signs of epithelial proliferation, such as erosion and leucoplakia, have been recognized as precancerous, at least to the extent that their treatment as a prophylactic measure is now enthusiastically recommended. For adenocarcinoma, however, no such theoretic or practical conclusions have been reached. The development of carcinoma from endometrial polyps has indeed been frequently reported but the existence of a relationship between cancer and endometrial hyperplasia, the disease which from analogy with similar conditions elsewhere might be regarded with immediate suspicion, has been denied by several writers.

Clinical experience with several striking cases in which the pathologic reports from a series of curettings from the same patient indicated an apparent transformation of hyperplasia to carcinoma led us at the Roosevelt Hospital to believe that the conclusions of these writers were perhaps premature. This opinion was strengthened by the finding in the literature of several similar cases and it was therefore decided to investigate the problem by a comprehensive survey of the clinical and pathologic material of the gynecological division relevant to the subject. For this

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purpose a review was undertaken of the adenocarcinomas of the corpus for twenty-one and a half years (Jan. 1, 1910 to July 1, 1931), of the benign endometrial hyperplasias for five years, and of the endometrial polyps for six years. The material studied comprised the following cases:

Hyperplasia of the endometrium	85
Endometrial polyps	50
Carcinoma of the corpus	152
Cases incorrectly diagnosed hyperplasia	128

I. EVIDENCE DERIVED FROM A STUDY OF CASES OF HYPERPLASIA OF THE ENDOMETRIUM

1. The Problem of Correct Diagnosis of Glandular Hyperplasia.—The work of reviewing the microscopic material had scarcely begun when it became clear that the problem, at least so far as the Roosevelt Hospital was concerned, depended upon the correction of diagnosis by the definition of the morphologic characteristics of glandular hyperplasia and its clear separation from physiologic forms of hypertrophy on the one hand and from early carcinoma on the other.

During the five-year period, 1925-1929, the diagnosis of hyperplasia or hypertrophy, or the apparently synonymous terms, hyperplastic or hypertrophic endometritis, were applied to 257 specimens of which, after extensive resectioning of material, 216 were available for satisfactory microscopic review. Of this number only 88 (from 85 patients) could probably be properly classed as glandular hyperplasia, the remainder being divided as follows: Normal premenstrual endometrium, 67; endometrium of the sixteenth to the twentieth day type, 19; endometrium of the early part of the interval, 19; endometrium of very early intrauterine pregnancy or in association with an ectopic pregnancy, 11; endometrial polyps, 7; basal layer hyperplasia with functioning endometrium, 2; carcinoma, 3. The histologic study was made with constant reference to the clinical history and the revised diagnosis was corroborated in almost every instance by the data upon types and dates of menstrual periods.

In many of the discarded cases, the error in original classification was due merely to a loose employment of the term hyperplasia by its application to a special physiologic phase of the endometrium, whereas in a few instances there was evidence of actual failure to recognize the nature of the tissue under examination. This group of cases forms the basis for casting the first doubt upon the validity of some of the apparent transformations of hyperplasia to carcinoma, for it is probable that in many general hospitals, where the pathologic work is carried on by departments neither particularly versed nor interested in special gynecologic problems, the term endometrial hyperplasia has very little significance.

2. Histologic Similarity of Endometrial Hyperplasia and Carcinoma.

—Shaw has written that he believes there is no relationship between

hyperplasia and carcinoma because he can see no histologic similarity of the endometrium in the two diseases. Meyer, on the other hand, has repeatedly emphasized that the morphologic distinction between hyperplasia and carcinoma is dependent upon differences of degree only and that there are cases which are practically transitional. Ewing writes in a similar vein that "in a series of cases [of hypertrophic endometritis] every gradation may be observed from normal glands to those of adenoma malignum."

The 85 cases in the present series may be collected into four ill-defined groups to illustrate this conception of a varying degree of hyperplasia which ultimately reaches a grade hardly distinguishable from the proliferative activity of a differentiated carcinoma. The relative frequency of each group is shown in Table I.

TABLE I. TYPES OF TREATMENT IN ENDOMETRIAL HYPERPLASIA

	HYSTER- ECTOMY	CURETTAGE AND RADIUM	CURETTAGE AND MYOMECTOMY	CURETTAGE AND OOPHORECTOMY	CURET- TAGE	TOTAL
1. Mild Hyperplasia	4	5	0	0	4	13
2. Moderate Hyperplasia 3. Marked	9	20	0	1	11	41
Hyperplasia 4. Excessive	7	13	1	1	3	25
4. Excessive Hyperplasia	3	2	0	0	1	6
Total	23	40	1	2	19	85

1. In the first type actual hyperplasia of the epithelium is very slight, the change from the normal consisting in the presence of a few cystic or distorted glands. Suggestions of cyclical activity may even be present, so that this group perhaps contains some uncertain cases.

2. The second group includes those with the typical "Swiss cheese" gland pattern with acini of varying size, lined by flattened or cuboidal cells. Evidences of proliferation are here slight, the presence of cystic glands being still the chief feature. It might therefore be preferable to term these cases dysplasia, as Graves has suggested, were it not for the apparently unbroken transition of this variety into the ensuing ones.

3. To the third group also belong cases commonly recognized as glandular hyperplasia, but here in addition to the irregular cystic changes there occur acini in which the epithelium is no longer flattened but is composed of large, closely approximated, high cylindrical cells. Clusters of small gland sections appear scattered through the stroma, suggesting new formation and perhaps complicated branching of glands (Fig. 1). In these cases a more definite hyperplasia has been added to the "dysplasia" of the other types.

4. There are finally a few cases whose structure has many of the features of carcinoma. In these the glands are no longer truly cystic, although they may exhibit marked variations in size, some being small and round, others flattened, still others large and distorted (Fig. 2). The epithelial band bordering the acini is greatly thickened, the nuclei lying at different levels in the cells so that the appearance is given of a

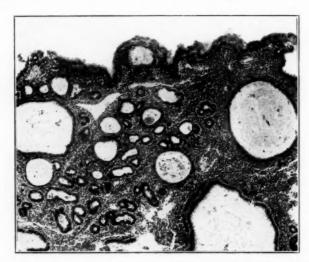


Fig. 1.—Hyperplasia of the endometrium in a woman of forty-four after two months intermittent bleeding (photomicrograph $\times 45$).



Fig. 2.—Hyperplasia of the endometrium in a woman of forty-six after seven years of nearly constant bleeding (photomicrograph $\times 70$).

multilayered epithelium (Fig. 3). The nuclei themselves vary considerably, but they are sometimes large with dark granules and the distinct nucleolus which Broders has described as of significance in the recognition of malignancy (Fig. 4). A tendency to the formation of intraglandular projections is present in certain cases (Figs. 2 and 5), and in others there are occasionally encountered suspicious areas of atypically staining epithelium (Fig. 5). In the latter, however, the possibility of a localized functional reaction, possibly an attempt at secretion, cannot be positively excluded. The cases of this fourth group are comparatively

rare but are of considerable importance in diagnosis and their easy confusion with carcinoma has led Heyman to question the accuracy of reported results in the treatment of cancer of the corpus unless the pathology has been carefully considered.



Fig. 3.—Hyperplasia of endometrium associated with fibrosarcoma of the ovary in a woman of fifty-five, with recurrent bleeding six years after the menopause (photomicrograph $\times 65$).

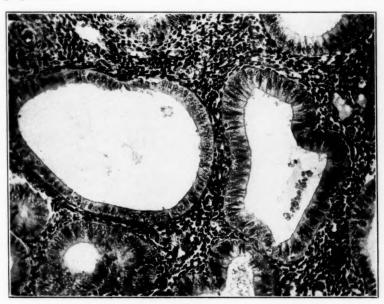


Fig. 4.—The epithelium in case of marked hyperplasia in woman of fifty-two (photomicrograph $\times 200$).

- 3. Biologically Similar Properties of Hyperplasia and Carcinoma.—In several respects the behavior of hyperplastic endometrial tissue is suggestive of that of careinoma.
- Tendency to Invasion: The observation has been made by several writers that in cases of hyperplasia the upper muscular layers are fre-

quently invaded by endometrial glands and stroma, constituting a condition termed adenomyosis. Shaw found this in all cases in which he had sections of the line of division between mucosa and muscle. Beckman reported adenomyosis interna in 6, a few penetrating glands in 7 and a sharp boundary in 7 of the 20 cases he studied. Novak and Martzloff noted adenomyomas in 8 of their 32 uteri in which there was hyperplasia of the mucosa.

In 19 of our cases sections were available for a study of the upper layers of the muscularis. In practically all, occasional glands were observable below the most superficial muscle fibers, while in 8 there were definite small islands and in 3 extensive areas of glandular tissue in the muscularis. The significance of these findings is perhaps not great, since a moderate degree of adenomyosis is almost the rule in women approach-

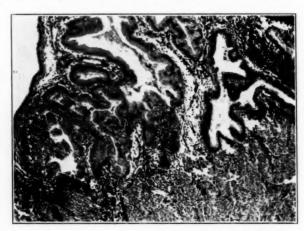


Fig. 5.—Areas of atypical staining reaction in same case as Fig. 4 (photomicrograph $\times 120$),

ing the climacteric (Meyer and Kitai). On the other hand, it is perhaps correct to regard the infiltrative capacity of these glands as the earliest foreshadowing of the invasive characteristics of carcinoma. It finds an analogy in the development of penetrating pegs of squamous epithelium described in leucoplakia of the cervix, the lesion alleged to be precancerous for that region (Hinselmann).

2. Tendency to Recur: It is well known furthermore that endometrial hyperplasia is frequently, perhaps as a rule, not cured by simple curettage, and when cures occur it is rarely in any except the milder cases. Fuss, for example, in a study of end-results, noted that among 17 mild cases, 13 were cured by curettage and 4 required x-ray afterwards, while among 14 moderate cases only 2 were successfully treated by curettage, and in 19 severe cases none were cured by curettage alone.

In the Roosevelt Clinic it is the custom to use moderate doses of radium very freely for bleeding in women over 40, and for that reason there are few cases to study in which the primary treatment has left much possibility for further endometrial activitiy. The frequency of recurrence in 12 cases treated by curettage only and observed for periods of one to six years may, however, be stated as follows: Mild hyperplasia, cured 1, recurred 2; moderate hyperplasia, cured 1, recurred 3; marked hyperplasia, cured 1, recurred 3; hyperplasia with borderline histology, cured 1, recurred 0.

4. Transformation of Hyperplasia to Carcinoma.—The actual derivation of a malignant tumor from a supposed precancerous lesion is difficult to prove, and in most instances of such apparent evolution one is unable to exclude the possibility of a mere coincidence of the two conditions. Nevertheless presumptive evidence exists that an actual transformation has taken place when there is a change in the histologic character of the curettings obtained from the same patient at successive operations. This happening has been referred to casually as of more or less frequent occurrence by several writers (Koblanck, McCann), but the specific instances that have been reported are rare.

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Extensive studies of the late results of treatment of hyperplasia have been made under the direction of Meyer in the University Clinic in Berlin, although here the aim has been frankly to test the efficiency of histologic diagnosis and not the possibility of carcinomatous evolution (Kaufmann and Hoeck, Mack, Fuss). Of special interest was a group of 24 cases of very marked hyperplasia in which there was a special fear of error (Hintze). None of the patients, whose subsequent history was traced, developed carcinoma, however, a fact indicative of careful original diagnosis as well as slight evidence against the malignant tendencies of hyperplasia.

Of the 85 cases originally diagnosed endometrial hyperplasia at the Roosevelt Hospital in the years 1925 to 1929, two later developed demonstrable carcinoma. On review both of these instances of apparent transformation were found to be due to original failures to detect the cancer. These cases were as follows:

Case 1.—W. P. A. Gynecologic history, 14028, 15881. First admission, December 14, 1925. Aged seventy-two, married, three children. Menopause at forty. Chief complaint, sanguineous discharge, duration four weeks. Operation, dilatation and curettage, insertion of radium, 50 mg. for ten hours. Gross findings, uterus normal size and position, curettings considerable in amount. Pathologic diagnosis, hyperplasia of the endometrium. Second admission, November 4, 1927. Chief complaint, discharge, one month duration. Operation, dilatation and curettage, complete abdominal hysterectomy, bilateral salpingo-oophorectomy. Gross pathology, uterus normal in size with two small papillary areas in the cavity. Pathologic diagnosis, adenocarcinoma, Grade I.

Study of the sections obtained from the first curettings confirmed the diagnosis of endometrial hyperplasia, but when new preparations were made from a deeper level in the paraffin block an island of papillary adenocarcinoma was discovered (Fig. 14).

Case 2.—E. L. Gynecologic history, 13593, 15343, 19303. First admission. November 7, 1925. Aged fifty-seven, single. Present illness: menstruation in this patient had been frequent, profuse and prolonged during her fifty-first and fiftysecond years, but had become infrequent at fifty-three and then ceased entirely until just before her admission. First operation, dilatation and curettage. Insertion of radium, 50 mg. for twelve hours. Gross findings, several small subserous fibroids, smooth eavity, curettings scant in amount. Pathologic diagnosis, hyperplasia of the endometrium. Second admission, May 20, 1927. Chief complaint, recurrence of bleeding, beginning about one year after the first operation. Second operation, dilatation and curettage, insertion of radium, 50 mg. for eighteen hours. Gross findings, uterus still slightly large and a little irregular, curettings moderate in amount. Pathologic diagnosis, hyperplasia of the endometrium. Third admission, June 24, 1930. Chief complaint, recurrence of bleeding at the age of sixty-three after a freedom from symptoms for three years. Third operation, complete abdominal hysterectomy, bilateral salpingo-oophorectomy. Gross pathology, uterus moderately enlarged, with small fibroids, the en-

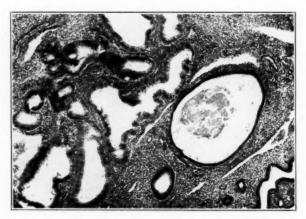


Fig. 6.—Hyperplastic glands in an endometrial polyp, associated with diffuse hyperplasta, in a woman of fifty-five, six years after the menopause (photomicrograph ×70).

tire eavity having a granular appearance. Pathologic diagnosis, adenocarcinoma, Grade I.

The sections obtained from the uterus after the final operation show a typical differentiated adenocarcinoma. The histology of the earlier curettings was essentially the same, the diagnosis of hyperplasia being an error made possible by the minuteness of the fragment in one instance and to poor staining in the other.

These two cases, which had afforded the original impetus to this study, illustrate the practical dangers of a confusion of hyperplasia and carcinoma due to a failure of the malignant parts of the endometrium to reach the microscope or to an erroneous interpretation of morphology. They emphasize furthermore the criticism that must be applied to cases of apparent evolution of carcinoma from hyperplasia.

5. Relation of Endometrial Polyps to Hyperplasia and to Carcinoma of the Endometrium.—Study of 50 cases of endometrial polyps treated in the years 1925-1930 brought out the already recognized relationship which exists between these growths and endometrial hyperplasia. In the

first place an associated generalized mucosal hyperplasia was found to be present in a third of the 18 cases of polyp in which the endometrium proper could be properly examined. Secondly, from a structural standpoint, it was noted that in 33 of these polyps the gland pattern was essentially that found in the diffuse disease and exhibited the same variations in degree of hyperplasia, from specimens made up of apparently inactive dilated cysts to others composed of closely packed, hypertrophied glands with small areas suggestive of active proliferation (Fig. 6).

No definite cancer was present in any of these cases, but the occurrence of carcinoma in endometrial polyps has been reported so many times that the malignant potentialities of these growths must be regarded as fairly well established (Stone, Stacy, Cooke, La Monica, Dannreuther). On account of the points of similarity, particularly those of structure, between these circumscribed and the generalized forms of endometrial hyperplasia, it seems logical to expect that carcinoma should at times arise on the basis of the diffuse hyperplasia also.

II. EVIDENCE OF ORIGIN FROM HYPERPLASIA IN A SERIES OF CASES OF CORPUS CARCINOMA

The review of the late results in a series of treated cases of hyperplasia has revealed little evidence of a tendency to the development of malignancy. Two possible objections to conclusions arrived at by this method of study may, however, be cited, one being that the interval of observation has been too short, the other that the cases were so thoroughly treated that possible potentialities for malignant change were adequately controlled. The approach to the problem from the opposite direction by a search of the histories of a series of cases of already existent carcinoma for evidence of a previous benign endometrial lesion and the pathologic material for evidence of coexistent hyperplasia has yielded many instances suggestive of a relationship.

A. EVIDENCE OF PREVIOUS HYPERPLASIA FROM THE HISTORY

Of the entire group of 152 cases of corpus carcinoma, there were only 128 in which any record of previous history was on file, so that percentages of frequency must be based on this number. In studying these cases particular attention was given to two points, first the history of an earlier curettage and, secondly the occurrence of metrorrhagia at the time of the menopause when irregular uterine hemorrhage is due in many cases to endometrial hyperplasia.

- 1. History of Previous Curettage.—Twenty-five patients (19 per cent) had been curetted at least once, prior to their admission for their carcinoma operation, for conditions other than miscarriage.
- a. Six patients were curetted within a year before their admission. Carcinoma was probably present at the time of the first procedure in all

of these, although in one case successive pathologic reports show an apparent change of a benign to a malignant neoplasm.

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b. Seven patients gave a history of curettage from one to four years before their final operation, this interval being long enough to indicate that cancer was either not present or else not discovered by the first operator.

W. P. A. The patient already cited as Case 1, who was curetted at the Roosevelt Hospital two years prior to her hysterectomy for carcinoma, the area of cancer having been missed originally by the microtome.

E. L. The patient already cited as Case 2, who was twice curetted at the Roosevelt Hospital before the nature of the tissue was correctly evaluated.

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It is certain that carcinoma was present in two and probably in the third of these cases at the time of the first operation. They illustrate the



Fig. 7.—Endometrium in a patient of forty-four, five years before operation for carcinoma. Cystic area (photomicrograph $\times 70$).

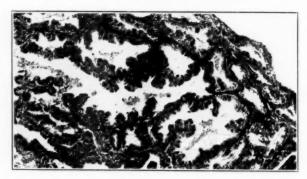


Fig. 8.—Endometrium in same case as Fig. 7. Papillary area (photomicrograph $\times 70$).

danger of inaccurate diagnosis as a result of incomplete curettage, incomplete sectioning, or bad pathologic judgment.

e. Four cases were curetted in the period between five and ten years before the operation for carcinoma. This interval makes it possible that in each case the earlier operation was performed for a benign condition and in the first instance to be reported pathologic sections of tissue obtained at the earlier operation are still available for study.

Case 5.—H. P. Gynecologic history, 19101. Admitted May 1, 1931. Aged forty-nine, married twenty-three years, no pregnancies. Chief complaint, irregular bleeding and continuous sanguineous discharge for twelve months. Previous history: five years ago the patient was curetted for brownish discharge by Dr. Herbert Thoms of New Haven, to whom I owe the privilege of publishing microphotographs of his original sections (Figs. 7 and 8). The pathologic diagnosis made in 1926 was symmetrical hyperplasia of the endometrium. Following this curettage the periods were normal until the onset of the present illness. Operation June 1, 1931, curettage and radium as a preliminary to hysterectomy. Gross pathology, the uterus slightly enlarged, the cavity containing a considerable quantity of friable tissue. Microscopic diagnosis, adenocarcinoma, Grade I.

Microscopic description: The curettings from the earlier operation show an endometrium of varying microscopic structure. In one region there are dilated glands of irregular shape lined by a single layer of large columnar cells (Fig. 6), while in other areas (Fig. 7) the glands have a papillary structure suggestive of a premenstrual endometrium. In comparison with the normal endometrium of the secretory phase, however, the cells of this papillary epithelium are large, with prominent nuclei, almost centrally placed, and a more deeply staining cytoplasm. Nucleoli are present in some of the cells but no mitotic figures. The tissue is certainly not an example of the classical glandular cystic hyperplasia although small areas with the structure of that disease are present. These earlier curettings apparently represent nevertheless an hyperplasia of some type, possibly an excessive degree of physiologic hypertrophy (Lahm, Adler, Meyer), possibly a kind of diffuse papillary adenoma. The sections obtained at the patient's second operation are those of a typical, rather highly differentiated papillary adenocarcinoma.

In a second case there is on record a pathologic diagnosis of hyperplastic endometritis made upon curettings obtained five years before the final operation for fundus carcinoma. No tissue or preparations have been preserved, however, and the extent of the growth at the final operation suggests an error in the earlier diagnosis.

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In the remaining two cases no pathologic diagnosis could be obtained from the earlier operation. The extensive character of the neoplasm when these patients finally came to hysterectomy indicates again that cancer may well have been present at the time of the first operations although such an explanation requires the supposition of a surprisingly slow rate of growth.

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d. Four cases were curetted over ten years before the operation for carcinoma. The first of these is apparently a clear example of the development of adenocarcinoma sixteen years after a curettage for endometrial hyperplasia. The diagnosis of hyperplasia is established by the detailed record of the type of bleeding, by the pathologic diagnosis and description and by the finding of a cyst in one ovary at celiotomy. That the cancer was a relatively late development is indicated by the scanty

menstruation and periods of amenorrhea which followed the early conservative operations.

Case 9.-H. S. Gynecologic history, 3096, 3298, 17761. Admitted, November 23, 1929, Aged forty-five, married, no children. Early menses normal, 28 by 3 days, worse. Previous history: the patient began when very young, to have menstrual difficulties and at the age of twenty-seven consulted Dr. Howard Taylor, Sr., on account of irregular, chiefly too frequent periods, and sterility. A curettage was performed at the Roosevelt Hospital on May 20, 1913, and a pathologic diagnosis of "chronic hyperplastic endometritis" made with the following description: "The endometrium shows a small round-cell infiltration. The glandular epithelium is somewhat hyperplastic, tending in places to heap up into several layers and the lumina of the glands are distorted and often dilated." A few months later the right tube and ovary were removed on account of an ovarian cyst, 8 cm. in diameter. During the next sixteen years, the patient was under observation at long intervals, her history showing that her periods were regular in 1915 (aged thirtyone), scant in 1917 (aged thirty-three), scant with months of amenorrhea in 1918 (aged thirty-four), profuse and of ten to twelve days' duration but at intervals of three to four months in 1923 (aged thirty-nine). The patient was then lost sight of until just before her present admission when she reported that her menses had remained irregular but not too profuse until the last few months when frequency and amount had increased. Operation (November 23, 1929), complete abdominal hysterectomy, salpingo-oophorectomy, left. Gross pathology: uterus, 9 by 6 by 4 cm. with its cavity lined by a shaggy growth extending from the fundus into the cervix. The left ovary contained a cystadenoma, serous in type, 12.0 cm. in diameter. Diagnosis, adenocarcinoma, Grade II.

In two other cases the nature of the original condition is less firmly established, but the type of symptoms, occurring at the menopause, makes it probable that in these also antecedent hyperplasia was present. The rather unusual types of malignant tumor later developing are, however, to be noted.

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The final case in this subgroup, however, weakens somewhat the conclusions drawn from the other three since here the course of the malignant disease impeded only by a curettage lasted over sixteen years.

Case 12.—M. T. Gynecologic history, 4352, 18610. Admitted, October 18, 1930. Aged sixty-one, single. Chief complaint, irregular bleeding for three months. At the age of forty-five, this patient was curetted at the Roosevelt Hospital for metrorrhagia. The pathologic diagnosis was adenomatous papilloma of the uterine mucosa but the note was added that such a type of growth, although not malignant, might become so. Sixteen years later there was found an extensive growth of the lower half of the uterus with the histologic structure of an adenocarcinoma, Grade II.

The sections from the curettage of 1914 are still available for study and show what would now be regarded as a differentiated type of adenocarcinoma. It is of course not clear whether cancer was continuously present in this uterus over a period of sixteen years or a new focus developed shortly before the return of symptoms.

e. Four cases were curetted early in life. These operations were performed under circumstances suggestive only of an abnormally developed

reproductive system or more specifically of some ovarian or endometrial disorder. In these patients (Cases 13 to 16, Gynecologic histories 14009, 16199, 16389, 17235), the operations had been performed, all before the age of thirty-five, for membranous dysmenorrhea, excessively painful menstruation, menorrhagia, and amenorrhea, respectively.

2. History of Previous Nonoperative Treatment of Symptoms Suggestive of Endometrial Hyperplasia.—Of the 128 cases of corpus carcinoma there were, beside the group that had had previous curettage, five cases which had been under medical observation for uterine bleeding at a time sufficiently remote from that of the operation for carcinoma to make it doubtful that a malignant tumor was then present.

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3. Previous History of Adenomatous Polyps of the Cervix.—It is interesting to note that of the 128 cases of corpus carcinoma, 11 gave histories of the removal of cervical polyps at some time prior to their final admission for cancer. The interval between the dates of treatment of the two lesions was from two weeks to two months in 4 cases, from six months to one year in 4 cases, eighteen months in 2 cases, seven years in one case, twenty years in one case. The polyps were not available for study to determine whether they were endometrial or endocervical in type, a point of some theoretical importance in considering their possible relationship to the endometrial carcinoma. From a practical standpoint, however, it is clear that the avulsion of a polyp with the omission of curettage is not an entirely safe procedure since valuable time was obviously lost in several of these cases as a result of the casual assumption that the polyp was the sole cause of bleeding.

B. THE ASSOCIATION OF HYPERPLASIA AND CARCINOMA IN THE SAME UTERUS

The morphology of the uninvolved endometrium in cases of corpus carcinoma has been little studied and what descriptions exist are extra-The controversy on this subject dates back at ordinarily conflicting. least to the writings of Gebhard at the close of the century and Maunu af Heurlin in 1911, both of whom held firm although completely conflicting views of the relation of "endometritis glandularis" to carcinoma. More modern work upon the problem has been largely limited to the reporting of special cases. Of greatest interest is a group of five cases described by Meyer, in which he demonstrated the fine morphologic line between hyperplasia and carcinoma and the occurrence of islands of cancer in areas of hyperplastic endometrium. The development of carcinoma in the hypertrophied glands overlying the most prominent points of submucous myomas has been noted in 3 cases by Ewing and in one by Doca, although it is not certain that this apparently localized hypertrophy is to be regarded as identical with the entity now known as glandular hyperplasia. There can, however, be little doubt of the association of hyperplasia and carcinoma in the cases noted by Schröder, by Adler and by Fluhmann and Stephenson. Yet Novak and Martzloff, in their paper on hyperplasia, have stated that "hyperplasia cannot be regarded as predisposing to cancerous growth" and Fluhmann and Stephenson consider their case of association as a mere coincidence since after a review of 22 other cases of carcinoma of the body no further evidence of hyperplasia could be found. This statement may be misleading, however, since the character of the endometrium in these 22 cases is not stated and it is not clear in how many uninvolved endometrium was present for examination.

The pathologic material for this study consisted of the filed microscopic sections of 130 and the gross specimens of 8 cases of corpus carcinoma. This material, when classified as in Table II on the basis of availability for microscopic examination of sections of endometrium uninvaded by cancer, rapidly dwindled so that only 11 cases were wholly satisfactory and 23 more partly so.

In regard to the condition of the endometrium in the fifteen cases with sections of only a little true mucosa (2a), no conclusive statements can be made. Nevertheless it appears that in 6 cases these glands were probably normal or atrophic, in 2 cystic, in 4 possibly hyperplastic and in 3 it is not clear whether certain groups of well formed glands are to be regarded as hyperplastic or as merely relatively differentiated areas of the carcinomatous process.

Table II. Availability of Sections of Nonmalignant Endometrium in Carcinoma of Corpus Cases

1.	Cases without sections of uninvolved mucosa]	104
	a. Advanced cases with entire cavity invaded 6	2	
	b. Cases treated by curettage or biopsy only 1	2	
	c. Cases previously irradiated	9	
	d. Mucosa present in gross but not sectioned 2	1	
2.	Cases with small areas of endometrial glands		23
	a. Cases with a little true mucosa 1	5	
	b. Cases with nonmalignant glands in polyps	2	
	c. Cases with nonmalignant glands in areas of adenomyosis	6	
3.	Cases with adequate endometrial sections		11

In two cases the only nonmalignant glands were localized in a polyp (2b). One of these polyps was uninvolved by carcinoma and must be considered an associated lesion, while in the other, cancer was present and had perhaps originated within the benign tumor. Reference has already been made to Stacy's finding of carcinoma in a polypus in 25 cases or 7.5 per cent of her series of fundus carcinomas.

Finally there were six cases in which the only nonmalignant mucosa remaining was that buried as islands of glands and endometrial stroma in the upper muscle layers. To these six must be added three more cases (Nos. 22, 26, 29) to be described below, in which intramuscular glands were present in addition to superficial areas of benign endometrium

(Figs. 9, 13). The presence of this adenomyosis in association with cancer has a distinct bearing on the subject since the invasive tendencies of these basal glands must be regarded as the manifestation of a hyperplastic process.

The eleven cases in which sections could be obtained with relatively large areas of noncancerous mucosa may be divided into the three following groups: (1) Those in which the associated mucosa was that of a normally functioning endometrium. (2) Those in which the mucosa showed evidence of hyperplasia and the women were of an age in which this disease is prevalent. (3) Those in which changes suggestive of hyperplasia were present in older women.

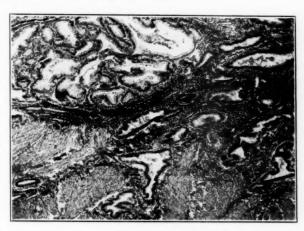


Fig. 9.—Adenocarcinoma of corpus with adenomyosis in the functioning endometrium of a woman of forty years (photomicrograph ×70).

1. Carcinoma in a Functioning Mucosa.—In two cases carcinoma occurred in a uterus with an essentially normal endometrium whose structure agreed with the day of the cycle as computed from the date of the last period. Both of these cases were very early ones and in neither had intermenstrual bleeding occurred. Yet in the first case, in spite of the evidence of normal function, there was present a rather marked degree of adenomyosis of the upper muscularis (Fig. 9). In the second no sections were available of the mucosal muscular boundary.

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2. Carcinoma Associated with Hyperplasia in Women at the Menopause.—In five cases of endometrial carcinoma occurring in women between the ages of forty-three and fifty-two there were evidences of benign hyperplasia in the uninvolved areas of mucosa. In two (Cases 26 and 28) the hyperplasia was of the rather typical cystic type, in two (Cases 24 and 29) the hyperplastic glands were very active, with irregularity in gland shape and in one (Case 25) the only remaining nonmalignant mucosa consisted in a very hyperplastic basal layer. The prob-

ability that these cases illustrate a development of carcinoma on the basis of a hyperplasia is heightened by the clinical point that the increased bleeding was in each case preceded by a longer or shorter period of lengthened interval in the menstrual cycle and perhaps also by the presence of cystic ovaries in three of the cases.

Case 24.—V. N. Gynecologic history, 7015. Admitted, May 27, 1917. Aged forty-three, married, one child. Original menstruation, 27 by 4. Present illness: menses began to occur every four to six weeks two years ago but for last seven months there has been intermenstrual bleeding also. Operation, dilatation and curettage, complete abdominal hysterectomy, bilateral salpingo-oophorectomy. Gross pathology, double uterine cavity with no fibroids, the carcinoma having been superficial and apparently all curetted away. Normal tubes. Cystic ovaries.

Microscopic description: the slide with the tumor was somewhat faded but showed an adenocarcinoma, apparently well differentiated. The areas of nonmalignant mucosa were composed of an edematous stroma with widely separated

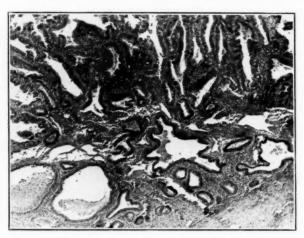


Fig. 10.—Superficial papillary adenocarcinoma overlying dilated and hyperplastic basal glands in a patient of forty-three years (photomicrograph $\times 60$).

glands which were irregular in size and shape, for the most part large and sometimes cystic and lined by closely approximated nonsecreting cylindrical cells.

CASE 25.—A. K. Gynecologic history, 11563. Admitted, September 26, 1922. Aged forty-three, married, four children. Original menses occurred every three to four months. Menopause at forty-one. Present illness: slight bleeding began six months ago and has recurred every three to four weeks. Operation, dilatation and curettage, complete abdominal hysterectomy, salpingo-oophorectomy, bilateral. Gross pathology, uterus normal size with a fungating growth beginning at the internal os and occupying the whole of the lower half of the corpus and partially invading the wall. Normal tubes. Cystic ovaries.

Microscopic description: the tumor was a papillary adenocarcinoma, Grade II. One section showed clearly a layer of basal endometrial glands beneath a narrow strip of superficial papillary carcinoma. The basal glands showed cystic dilatation and great irregularity of size and shape. Their cells were large and cylindrical but distinctly different in type from those of the carcinoma (Fig. 10).

Case 26.—C. U. Gynecologic history, 13212, 14431. Admitted, December 2, 1924. Aged fifty-one, married, two children. Original menses, 28 by 5. Previous opera-

tion, partial amputation of cervix for tuberculosis in 1910. Present illness: in 1919 when the patient was forty-six a fibroid was noted on a routine examination. Her periods were regular until 1921 when they occurred at two to three months intervals and were very scant. This type of irregularity was replaced by too frequent menstruation in 1922 but in the following two years the intervals were stretched out to as much as four months. Shortly before admission a continuous sanguineous discharge commenced. Operation, December 4, 1924, complete abdominal hysterectomy, bilateral salpingo-oophorectomy. Gross pathology, uterus

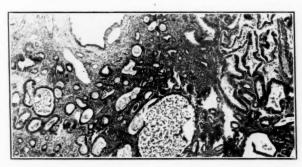


Fig. 11.—Adenocarcinoma adjacent to glandular cystic hyperplasia in a patient of fifty-one years (photomicrograph ×40).

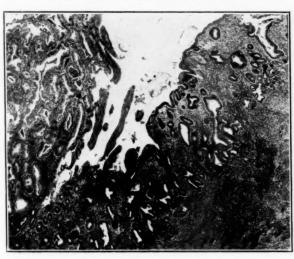


Fig. 12.—Papillary adenocarcinoma apparently arising from a hyperplastic endometrium in a patient of fifty-one years (photomicrograph ×40).

enlarged by about thirty fibroids, varying in size from 0.8 to 8.0 cm. in diameter. The adnexa showed numerous old adhesions, possibly the result of tuberculosis. In the lower uterine cavity there was a thickening of the endometrium and numerous polyps in the cervical canal. Microscopic diagnosis, chronic cystic endometritis, multiple fibromyomas, cervical polyps, bilateral chronic salpingitis and oophoritis. Subsequent course: a papillary growth developed in the vaginal vault two years later, a biopsy of which showed a typical adenocarcinoma, Grade II, endometrial in type.

Microscopic description: the sections on which the original diagnosis of chronic cystic endometritis was made had not been kept, due to the benign diagnosis. New

sections from the preserved paraffin blocks revealed an absolutely typical glandular cystic hyperplasia with in places large dilated glands lined by a flattened epithelium and in other regions numerous small, round and oval glands with large closely packed cylindrical cells. Beneath the superficial layers of muscle were islands of stroma and glands showing the same hyperplastic changes. Adjacent to the zone of hyperplastic mucosa was a region of definite carcinoma with malignant glands occupying the greater part of the thickness of the endometrium but separated from the uninvaded muscularis by a thin rim of flattened normal glands. The later recurrence of the carcinoma corroborates this diagnosis of malignancy (Fig. 11).

Case 27.—E. C. Gynecologic history, 16116. Admitted, February 24, 1928. Aged fifty-one, unmarried. Original menses, every twenty-one days. Present illness: six years ago periods stopped for six months and then returned to recur at two- to three-week intervals ever since, with great variation in duration and volume. Operation, complete abdominal hysterectomy, salpingo-oophorectomy, bilateral. Gross pathology: uterus enlarged by fibromyomas to measure 15 by

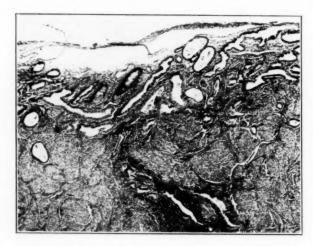


Fig. 13.—Hyperplasia of the endometrium with adenomyosis in a section remote from the carcinoma in a patient of fifty-two (photomicrograph ×60).

12 cm. with almost the entire cavity shaggy with papillary growth. Serous cyst of left ovary. Diagnosis, adenocarcinoma, Grades I and II.

Microscopic description: one section cut through the margin of the growth showed a relatively narrow strip of endometrium with its surface epithelium largely intact, containing many small glands and a few irregular-shaped dilated acini lined by an epithelium of one or two layers of high cylindrical glands. The appearance is not exactly that of the common cystic type of hyperplasia, but conforms with the description given of the more active types (Fig. 12).

CASE 28.—H. H. Gynecologic history, 17326. Admitted, May 26, 1929. Aged fifty-two, married, one child. Original menses, 28 by 5. Present illness: for seven years the patient's periods have been irregular, occurring every three to six months. For seven months there has been frequent scant bleeding. Operation: complete abdominal hysterectomy, salpingo-oophorectomy bilateral. Gross pathology: a uterus with several fibroids forming a mass the size of a grapefruit and in the eavity a "growth at one point near the fundus." Atrophic ovaries. Microscopic diagnosis, adenocarcinoma, Grade II.

Microscopic description: the sections of the malignant tumor were those of an adenocarcinoma, Grade II. Entirely separate sections showed a narrow strip of mucosa, composed of dilated glands, flattened, with their long axes parallel to the surface. Other glands were small and lined by large columnar cells, while still others were definitely cystic (Fig. 13).

3. Carcinoma Associated With Apparent Hyperplasia in Women Over Sixty.—Four cases of carcinoma in older women were found associated with proliferative changes in the endometrium of a less definite character than those just described. In one (Case 27) the hyperplastic features are chiefly cystic dilatation in the mucosa with endometrial islands in the



Fig. 14.—Adjacent islands of tissue obtained by curettage showing papillary carcinoma and hyperplastic glands in a patient of seventy-two (photomicrograph ×60).



Fig. 15.—Hyperplastic glands in the fibrous stroma of the uterine mucosa of a woman of seventy-five with carcinoma of the corpus (photomicrograph $\times 80$).

muscularis. In another (Case 31) there is a definite noncystic hyperplasia of the glands well beyond the apparent margins of the cancer, but perhaps these active acini should be regarded as merely the relatively differentiated beginnings of the carcinomatous process itself. The remaining two (Cases 28 and 30) with their greatly dilated cystic glands are morphologically similar to the more typical glandular cystic hyperplasias of the menopause era.

The atrophic condition of the ovaries in these elderly women makes it possible that the endometrial activity has here a different origin than that of the classical hyperplasia of the premenopausal era. In this re-

spect Hofbauer's experiments on the relation of the anterior pituitary to endometrial hyperplasia offer an opportunity at least for speculation. It is likewise possible, however, that the endometrial abnormalities in these older women are but remnants of a typical hyperplasia persistent since the menopause.

V. A. Gynecologic history, 14028, 15881. Admitted December 4, 1925, and November 4, 1927. Aged seventy-two and seventy-four. The clinical data on this patient have already been given as Case 1.

Microscopic description: As has been noted, a small area of papillary adenocarcinoma was found upon recutting the sections of the tissue diagnosed in 1925

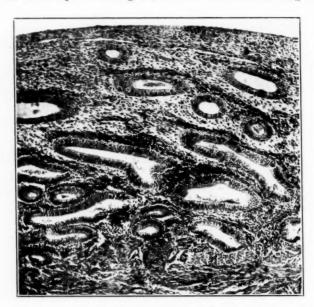


Fig. 16.—Section through the endometrium, 5 mm. from the margin of a papillary adenocarcinoma of the corpus in a patient of sixty-seven years (photomicrograph $\times 80$).

only as hyperplasia. The nonmalignant areas of endometrium from that year showed a stroma very fibrous in character containing numerous immensely dilated glands. The epithelium of the glands was high columnar, with oval nuclei crowded close together, apparently forming in some places more than one layer (Fig. 14). The tissue of two years later showed a similar dense stroma and even larger acini with irregular wavy contours adjacent to patches of infiltrating carcinoma. The ovaries were recorded as being atrophic.

Case 29.—M. S. Gynecologic history, 16207, 16722. Admitted, October 28, 1928. Aged sixty-four, married, at least one child. Menopause at fifty-three. Present illness: the patient noted a little vaginal bleeding eight years ago and again six months ago. Following the latter attack a cervical polyp was removed but bleeding has continued. Operation, complete abdominal hysterectomy, salpingo-oophorectomy bilateral. Gross pathology: uterus enlarged by numerous fibroids with a small walnut-sized growth in the cavity at the fundus. Diagnosis, adenocarcinoma, Grade I.

Microscopic description: The endometrium was narrow and somewhat atrophic, with here and there immense very thin-walled cysts. Associated with the cysts were

clusters of flattened glands which in places dip down into the muscle tissue and in several areas form islands of glands and stroma in the myometrium.

Case 30.—J. K. Gynecologic history, 17443. Admitted, September 5, 1929. Aged seventy-five, married, eight children, menopause at forty-three. Present illness: for four years the patient has suffered from irregular bleeding with the amount gradually increasing. Operation, dilatation and curettage, supravaginal hysterectomy, bilateral salpingo-oophorectomy. Gross pathology, uterus two and one-half times normal size, soft and boggy, with one intramural fibroid and a large submucous polypoid tumor. Ovaries, small and fibrotic. Diagnosis, adenocarcinoma, Grade II.

Microscopic description: The uninvolved endometrium is very similar to that noted in Case 29 with a fibrous stroma and immense dilated glands, some lined by a flattened, apparently atrophic epithelium, others by high columnar cells. Besides cystic acini there are smaller tubules, some in clusters, others single and irregular or tortuous in shape (Fig. 15).

Case 31.—W. H. C. Gynecologic history, 18951. Admitted, March 19, 1931. Aged sixty-seven, married, one child. Menopause at fifty-two. Present illness: a cervical polyp was excised one year ago but irregular bleeding recurred eight months ago and has continued. Operation, dilatation and curettage, complete abdominal hysterectomy, salpingo-oophorectomy bilateral. Gross pathology, uterus slightly enlarged with growth filling the upper half of the cavity. Ovaries atrophic. Diagnosis, adenocarcinoma, Grade II.

Microscopic description: One section included a small segment of the tumor, which was a papillary adenocarcinoma, and a larger area of uninvolved mucosa. The endometrium immediately adjoining the base of the tumor was atrophic, possibly from pressure, but further away it widened out to form a definite though somewhat narrow strip just above the myometrium. The glands were perfectly regular except for a few in the basal layer which showed slight invaginations. The epithelium was high columnar with definite multiplication in some places of the cell layers. The individual cells were, however, smaller and more cylindrical and the cell boundaries more distinct than in the areas of carcinoma (Fig. 16).

C. ETIOLOGIC POINTS OF DIFFERENCE AND SIMILARITY

A few points in the etiology of hyperplasia and carcinoma rest on a basis sufficiently firm to demand their consideration in studying any suggested relationship between the two diseases.

SUMMARY

The relationship of hyperplasia to carcinoma of the endometrium has therefore an etiologic and a clinical aspect.

I. Etiologic relationship: The position of endometrial hyperplasia as a precancerous lesion rests upon the following evidence:

1. Morphologic similarity: The weight given such evidence is largely dependent upon individual conception of form and is not susceptible to direct proof. A review of 85 cases of endometrial hyperplasia suggests, however, that this entity consists in reality of a series of types varying from those which differ little from normal endometrium to others which closely resemble certain differentiated carcinomas.

2. Biologic similarity. The frequent association of endometrial hyperplasia with adenomyosis or the invasion of the muscularis by mucosal tissue and the tendency of the disease to return after curettage are perhaps to be interpreted as representations in miniature of two of the chief properties of malignancy, infiltration and recurrence.

3. Transformation of hyperplasia into carcinoma, as indicated by a change in the character of the tissue obtained in successive curettings in the same patient, has been reported in the literature in at least six instances. Such cases must, however, be regarded critically because of the frequent lack of precision in the use of the term hyperplasia and the possibility that undetected carcinoma may have been present in the uterus at the time of the first operation. The only two instances occurring among 85 cases treated for hyperplasia of the endometrium at the Roosevelt Hospital from 1925 to 1929 of apparent transformation to carcinoma were dependent upon such errors.

A review of 122 histories in cases of corpus carcinoma brings out the fact, however, that very many of these women had at some time before their final operation for cancer been under treatment for abnormal uterine bleeding. These cases may be divided as follows:

a. Cases in which endometrial hyperplasia almost certainly preceded carcinoma (Cases 5, 9).

b. Cases in which the time and characteristics of the previous bleeding make it probable that a period of benign endometrial disease preceded the development of the malignant tumor (Cases 10, 11, 18, 20).

c. Cases in which the earlier condition was obviously regarded by the clinician or pathologist as benign but which subsequent events indicate was very likely malignant (Cases 3, 4, 6, 7, 8, 17, 19, 21).

d. Cases in which the earlier bleeding was later definitely proved to be due to an unrecognized malignant growth (Cases 1, 2, 12).

4. The association of diffuse endometrial hyperplasia and carcinoma in the same uterus has been reported by previous observers and was noted in five instances (Cases 24, 25, 26, 27, 28) in the present cancer series. Similar proliferative changes were observed in 4 cases (Cases 1, 29, 30, 31) in women over sixty, in which, on account of the patient's age the unqualified use of the term endometrial hyperplasia has been withheld. In two further instances the carcinoma occurred with hyperplastic glands which were probably a part of an adenomatous polyp. Finally there were 9 cases of carcinoma associated with areas of invasion of the superficial muscularis by benign glands, constituting a condition termed adenomyosis and indicating abnormal properties in the basal endometrial glands.

Although in a total of 152 cases there were only 15 with definite histologic evidence of an associated hyperplastic condition of some type, one cannot speak in terms of percentages, since it is obvious that many cases are so advanced that possible benign preexistent lesions have been completely displaced by carcinoma.

- II. Clinical relationship. Several cases in this series indicate that even with thoughtful handling, endometrial cancer may be mistaken for a benign condition. These cases lead to the following more or less obvious conclusions:
- 1. Postmenopausal bleeding from the uterine canal even if limited to a single attack should always be treated by curettage. No period of observation is sufficient to give security because further clinical evidence of carcinoma may not appear for even ten years after such an attack (Cases 17, 18, 19).
- 2. Curetted material, no matter how scant, may be carcinomatous, and it is never justifiable to dispense with microscopic examination (Case 7).
- 3. An incomplete curettage is not satisfactory as a diagnostic measure, for a small carcinoma may be missed by the instrument.
- 4. A single microscopic section of curettings is not sufficient to rule out cancer in suspicious cases because the microtome may not cut the particle containing the growth (Cases 1 and 26).
- 5. The histologic differentiation of hyperplasia from certain types of carcinoma requires at times considerable experience and the examination of multiple sections. The possibility of errors in diagnosis is very real and mistakes may lead to disastrous results (Cases 2, 12, and possibly 3, 4, and 6).

Whether from a practical standpoint hyperplasia is to be regarded as precancerous and treated as such must remain an open question. The relative frequency of hyperplasia undoubtedly indicates that the individual patient with the disease is reasonably safe. Nevertheless it appears that when the hyperplasia is at all marked, the possibility of a predisposition to the development of cancer should be considered and the case regarded with the same degree of suspicion now bestowed upon the diffuse forms of hyperplasia of the breast epithelium. In patients of the menopause age and older an adequate dose of radium is particularly indicated, certainly as the most efficient method of controlling bleeding, possibly as a prophylactic measure against the development of cancer.

REFERENCES

Adler, L.: Biol. u. Path. d. Weibes, Halban-Seitz 4: 135, 1928. Babes, A. A.: Arch. f. Gynäk. 122: 448, 1924. Bäcker, J.: Zentralbl. f. Gynäk. 28: 735, 1904. Beckman, M.: Arch. f. Gynäk. 135: 519, 1929. Broders, A. C.: Ann. Surg. 58: 141, 1921. Cooke, W. R.: Am. J. Obst. & Gynec. 19: 210, 1930. Dannreuther, W. T.: Am. J. Surg. 8: 824, 1930. Doca, V.: Ztschr. f. Geburtsh. u. Gynäk. 58: 1, 1906. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, 1928, Saunders, p. 597. Fluhmann, C. F., and Stephenson, H. A.: Surg. Gynec. Obst. 48: 425, 1929. Fuss, E. M.: Zentralbl. f. Gynäk. 49: 404, 1925. Gebhard, C.: Pathologische Anatomie der weiblichen Sexualorgane, Leipz., 1899, Hitzel, p. 154. Graves, W. P.: Tr. Am. Gynec. Soc. 55: 234, 1930. Heyman, J.: Strahlentherapie 37: 254, 1930. Hintze, O.: Zentralbl. f. Gynäk. 53: 2396, 1929. Hirst, B. C.: Am. J. Obst. & Gynec. 18: 104, 1929. Hitschmann, F., and Adler, L.: Monatschr. f. Geburtsh. u. Gynäk. 27: 1, 1908. Hofbauer, J.: Zentralbl. f. Gynäk. 54: 2569, 1930. Horsley, J. S.: Am. J. Obst. & Gynec. 7: 106, 1924. Kaufmann, K., and Hoeck, W.: Ztschr. f. Geburtsh. u. Gynäk. 90: 594, 1927. Koblanck, H. J. A.: Handb. d. Gynäk. (Veit) 3: 649, 1908. Lahm, W.: Zentralbl. f. Gynäk. 49: 698, 1925. Monatschr. f. Geburtsh. u.

Gynäk. 82: 157, 1929. McCann, F. J.: Proc. Roy. Soc. Med. 13: 3, 1919. Mack, H.: Zentralbl. f. Gynäk. 53: 2068, 1929. Maunu af Heurlin: Arch. f. Gynäk. 94: 402, 1911. Meyer, R.: Ztschr. f. Geburtsh. u. Gynäk. 85: 441, 1923. Idem: Zentralbl. f. Gynäk. 49: 1662, 1925. Idem: Ztschr. f. Geburtsh. u. Gynäk. 95: 178, 1929. Idem: Zentralbl. f. Gynäk. 53: 1362, 1929. Meyer, R., and Kitai, I.: Zentralbl. f. Gynäk. 48: 2449, 1924. La Monica, U.: Policlinico (sez. chir.) 37: 1, 1930. Novak, E., and Martzloff, K. H.: Am. J. Obst. & Gynec. 8: 385, 1924. Schröder, R.: Arch. f. Gynäk. 104: 27, 1915. Idem: Monatschr. f. Geburtsh. u. Gynäk. 58: 294, 1921. Also in: Zentralbl. f. Gynäk. 46: 195, 1922. Shaw, W.: J. Obst. & Gynec. Brit. Emp. 36: 1, 1929. Stacy, Leda J.: Surg. Gynec. Obst. 49: 43, 1929. Stone, W. S.: Surg. Gynec. Obst. 23: 248, 1916. Taussig, F. J.: Surg. Clin. 5: 1437, 1925. Te Linde, R. W.: South. M. J. 23: 571, 1930.

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(For discussion, see page 439.)

THE TREATMENT OF CARCINOMA OF THE CERVIX BY VAGINAL HYSTERECTOMY AND RADIUM*

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DESIRE to present herewith an account of my methods of treatment for cancer of the cervix. The discussion of this subject of therapy seems to me vital for two reasons: (1) The incidence of collum carcinoma has in the last five years shown a remarkable increase. Cancer is unlike that common malady, tuberculosis, which in the past few years has decidedly decreased. Cancer mortality has increased so decidedly that, because of these figures, we must consider carcinoma as a widespread malady. (2) Another cause, which in my opinion makes cancer a theme worthy of discussion, is that we are apparently at the turning point in its treatment.

TABLE I. FEMALE MORTALITY STATISTICS IN VIENNA*

DIED IN THE YEAR	1924	1925	1926	1927	1928	1929
Lung Tuberculosis	1446	1299	1249	1256	1113	1074
Malignant Tumors	1625	1721	1811	1907	1903	1997
From this malignant tu- mor group: cancer of the female sex organs	425	438	471	521	535	548

*Number of deaths from Tuberculosis decreasing, from Cancer increasing. Of all the cases of the female sex organs about 75 per cent are cancers of the cervix uteri.

At the beginning of this century the Wertheim abdominal cancer operation was in universal use, and the vaginal cancer operation previously in use was almost completely abandoned. The Schauta Clinic alone adhered to the vaginal carcinoma operation, which we attempted to extend and to make more radical. The reason for our fidelity to the vaginal carcinoma operation, which we attempted to extend and to make more radical.

^{*}Read by invitation at the Forty-fourth annual meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, White Sulphur Springs, W. Va., September 14-16, 1931.

nal radical operation was the enormous mortality of the laparotomy which we had not to fear with the vaginal procedure. This enormous death rate on the one hand, coupled with the relatively unsatisfactory permanent cure on the other hand, was the reason which induced a number of gynecologists shortly before the War to abandon the operation and to treat earcinoma of the uterus with radiation only. Originating with the French this method was first recommended by Krönig and Döderlein.

The results of the radium treatment were at first much worse than those of the operation. This was not sufficient to divert the adherents of the radiation therapy, for they maintained, and rightly so, that the technic of radiation was as yet not fully developed and that one could not fairly compare its results with those of the highly advanced surgical procedures. In the year following the War, the western countries, chiefly France (Regaud-Monod), Belgium, England and particularly America, devoted themselves to the nonsurgical treatment of carcinoma of the cervix. On the other hand, prominent men in Germany, Austria, Spain, and Poland have again upheld the vaginal radical operation. Thus, we have at our disposal today three different methods of cancer treatment: (1) laparotomy, (2) vaginal operation, and (3) radiation. All three methods after a test period of from fifteen to twenty years have by now outgrown their infancy and are at such a height of development that they permit a satisfactory comparison. Only on the basis of this comparison will the conscientious investigator be able to decide which method of cervix carcinoma treatment he should employ.

Before we take up the details of this comparison, it seems necessary to state clearly certain fundamental rules of cancer statistics. gynecologists have agreed that before we call a case of carcinoma cured, at least five years must have elapsed since the end of treatment (either operative or radiation therapy). If the patient lives five years free from recurrence, then we speak of a "permanent cure." Among the permanently cured, we differentiate between "relative" and "absolute" cures and we form the relative percentage by comparing the number cured after five years with the number of the operated. For instance, if Operator A has operated upon ten women and, if after five years, four of these patients will live he has a relative cure percentage of 40. If Operator B has operated upon ten women of whom eight still live, he has a relative cure percentage of 80. These figures seem at first sight to show that Operator B has a more successful operative result than Op-This conclusion would, however, be reliable only if both operators had the same indications, that is, if both had the same opera-Therefore, in order to make possible a comparison of the relative cures, every operator must declare his percentage of operability, otherwise one can not make deductions from the conception of the relative To retain the same example, if Operator A in his indication for operation goes so far as to operate upon ten women out of twenty, his relative cure of 40 per cent actually implies a much greater accomplishment than that of Operator B, who only dares to operate upon the early eases and, for example, operates upon only ten out of 100 cases, although the relative cure of Operator A amounts to 40 per cent and that of Operator B to 80 per cent.

To be independent from the subjectivity of the indication and thus to establish a really reliable means of estimating the worth of a method, an absolute cure must be understood to mean that number which indicates how many out of a hundred women (including both operable and inoperable cases) are still alive and free of recurrence after five years. According to this principle the absolute accomplishment of Operator A amounts to 4 out of 20, which is 20 per cent, and that of Operator B amounts to 8 out of 100, which is only 8 per cent. It actually shows that Operator A, whose operative cure percentage amounts to 40, has more than the double result of Operator B, in spite of the fact that Operator B's relative cure percentage amounts to 80.

A further idea which is very decisive in establishing the worth of an operative method is that of the primary death rate or operative mortality, that is, the percentage of women who die from the operation or its consequences. It is clear that with an equal number of permanent cures I shall give preference to that method of operation where I have to consider a smaller mortality.

TECHNIC OF VAGINAL OPERATION

Before comparing the results, I want to demonstrate briefly our technic of the extended vaginal operation. We begin with the excochleation and cauterization of the ulcerated tumor which is sometimes done the day before the operation. This is important because the danger of infection is lessened. The operation is commenced with a circular cut in the middle or lower part of the vagina, sometimes at the entrance according to the extension of the newgrowth. The mucous membrane is then dissected up as a cuff which is closed by thick silk sutures to exclude the newgrowth from the field of operation and from the wounds in the cellular tissue. A deep paravaginal (Schuchardt) incision, which cuts the levator ani, is then made. The bladder is next dissected from the cervix, first in the middle, then laterally, after which the most important part of the operation, namely, the dissection of the ureters is systematically performed. Great care has to be taken especially in cases of carcinomatous infiltration of the parametrium. After the dissection of the ureters, the uterine arteries are ligated. By pulling forward the uterine vessels with a provisional ligature, it is possible to place the ligature around the artery outside the ureter. In some cases the ureter is so involved in the growth that it can not be separated and so has to be resected. In these cases I have at once implanted the ureter into the bladder by the vagina, but the final results are not very satisfactory: most of these patients die after a few years, of recurrence. After the dissection of the ureters and bladder they can be pushed off with a retractor so that the parametrium is visible in its total extension. The rectum is then dissected from the cervix, and the pouch of Douglas is opened. The parametrium is next extirpated, first the sacrouterine ligament. This ligament is pulled forward with strong forceps and cut clear at the pelvic wall. The arteria hemorrhoidalis is then clamped with forceps. After the posterior parametrium has been incised, the lateral parametrium is pulled forward and out at the pelvic wall. At this part of the operation, the dissected ureter is always seen and is pushed back with the retractor, and the rest of the parametrium close to the uterine arteries is extirpated. As the uterine vessels have been previously ligated, there is very little hemorrhage. Therefore, there is no need for ligature or clamp and the parametrium is cut freely. This is of great importance, because it allows the whole parametrium to be removed without leaving a stump which might contain carcinoma cells. The same procedure is used on the other side. It is astonishing how a parametrium seemingly absolutely stiff and rigid from infiltration becomes movable during the operation. The anterior plica of the peritoneum is now opened and the uterus hangs on the round ligaments and adnexa only, which I always extirpate. The uterus is removed in the usual way at this stage. The peritoneum is closed, the stump of the infundibulopelvic ligament being pulled out and fixed with a suture so that all stumps are placed extraperitoneally. When doing this it is necessary to remember the situation of the ureter because it can be caught with the last stitch. This is the technic which has been used in the last 800 cases though sometimes modified in details according to the particular conditions of the case.

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I have been scrupulously careful in compiling my statistics. All patients who died within the observation period of five years from intercurrent diseases are counted as recurrences unless the autopsy report stated un-

TABLE II. REPORT OF 1000 CASES OF EXTENDED VAGINAL OPERATION*

YEARS	OPERABILITY	DIED FROM OPERATION
	52.79%	6.1 %
1901-1906	47.5 %	11.37%
1906-1911	55.45%	6.4 %
1911-1916	53.26%	4.34%
1916-1921	51.55%	3.51%
1921-1927	61.7 %	3.88%

^{*}All Wertheim cases are counted as inoperable.

TABLE III. FIVE YEAR CURES*

YEARS	OF THE OPERATED (RELATIVE)	OF ALL CASES (ABSOLUTE)
1901-1906	35 %	16.6%
1906-1911	37.89%	20.4 %
1911-1916	43.3 %	22.5 %+
1916-1921	43.0 %	21.99%
1921-1927	50.0 %	31.8 %++

^{*}The laparotomies and untraced cases are considered as recurrences.

^{+,} Radiations after operation began. ++, Almost all radiated after operation.

questionably that no carcinoma recurrence was to be found. Also, all patients who were not available after five years, the so-called "lost track of" patients, are considered as recurrences. Likewise in this table of statistics, the aim of which is to show the capacity of the vaginal operation, all cases are counted as recurrences in which for one reason or another the laparotomy instead of the vaginal operation was performed.

Before comparing the results of the abdominal and vaginal cancer operations I want to show you the progress in the outcome of the first 1000 cases of vaginal operation (the total number will be about 1200 now). Table II shows that the operability varies from 47.5 per cent to 61.7 per cent; the primary mortality being about 11.5 per cent in the first cases, gradually going down to 3.8 per cent, with an average of 6 per cent in 1000 cases (3.6 per cent in the last fifteen years). The relative cure percentage varies from 35 per cent to 50 per cent, and the permanent cure percentage from 16.6 per cent to 31.8 per cent.

Comparing now the results of the leading operators by the abdominal route (Wertheim and Bonney) for the last fifteen years we see that the vaginal operation with almost the same, and an even somewhat larger,

TABLE IV. RESULTS OF RADICAL OPERATIONS DURING THE LAST FIFTEEN YEARS

	ABDOMINAL		VAGINAL	
	WERTHEIM	BONNEY	SCHAUTA	
Operability	51.1 %	63.0 %	57.05%	
Died of operation	16.0 %	16.6 %	3.85%	
Five year cures of the operated (relat, cures)	39.2 %	39.63%	41.7 %	
Five year cures of all cases (absol. cures)	18.56%	25.00%	21.63%	

Table V. Results Following Treatment of Cancer of the Cervix, With Permanent (Five Year) Cures

RADIA	ATION		OPER	RATION		
WORLD LITERATURE (FRANQUE)	CASES 6827	ABSOLUTE CURES 17.45%	WORLD LITERATURE (HEYMAN)	CASES 5816	ABSOL CURES 1	
Döderlein	1319	15.4% (18.2%)	Wertheim (Lap.)	1000 500	18.56 20.0	
Wintz	740	18.9%	Bonney (Lap.)	265	25,0	%
Forsell-Heyman	502	23.3%	Franz (Lap.) (2 years)	9	28,3	%
Regaud	222	16.6%		200	10.0	01
Bowing-Fricke	1094	21.8% (23.0%)	Schauta (vaginal oper.)	698	19.8 22.5	
George Gray Ward	134	23.6%				

operability has a permanent cure of about 22 per cent. It involves a much smaller primary operative mortality inasmuch as on the average nearly four times as many women die after laparotomy than after our vaginal operation. (Table IV.)

If we compare now the results of operation with those of radiation therapy we have at our disposal large series of statistics. Döderlein figured out of a series of 1,319 cases a permanent cure percentage of 15.4 per cent and even by excluding the cases which were exposed to radium treatment only once, 18.2 per cent. Regaud, of the Paris Radium Institute, has an absolute cure rate of 16.6 per cent; Wintz with roentgen rays has an absolute cure of 21 per cent; Voltz figures from world literature for radium therapy rate of 17.4 per cent; Heyman, of the Radiumhemmet in Stockholm, figures from the world literature an absolute cure in surgical treatment of 19.1 per cent, and in the case of radiologic treatment in the Radiumhemmet of 23.6 per cent (Strahlentherapie, 39: 1930). This master is modest enough to say that with a properly executed radiologic treatment of carcinoma of the cervix one can have at least as good results as with operation. Herein lies, according to my opinion, a particular stress on the little word "proper," because the properly performed radium therapy is at least as difficult to learn as the operation itself. (Table V.)

The objective comparison of the figures from the world literature shows that the results of the radium therapy perhaps in the hands of an expert will be as good as the results of an operation, but in no case will they exceed the results of the operation. If we consider that the unsatisfactory results where the only reason why operation was abandoned and radiation tried, we must confess, that radiation has not advanced us any further in our fight against cancer than operation has done. In radiation we have a second means of attack against cancer, but no better.

Naturally this does not imply any underestimate of the men who have had the courage to give up the cancer operation and to replace it with radium therapy. Neither does it imply an underestimate of the very extraordinary success of radiation therapy, but it challenges us to search for other methods to improve our results.

If we consider operation first then we must endeavor to increase the number of permanent cures through greater radicalism. We attempted this in the Schauta Clinic, and we were so radical that the operability for a time was increased from 50 per cent to 78 per cent. The expected success was not forthcoming. We had the same experience that others subsequently had; with the increasing radicalism the danger of the operation and the mortality increased, likewise the number of recurrences increased but the permanent cures did not grow. That is the reason why I am in agreement with those who claim, that we can not improve the permanent cures by radicalism or by extending the indications for operation.

Where the lever must be applied to improve the results, we know ex-

actly. The statistics of both methods of treatment, operation and radiation, shows that in early selected cases we can save nearly 90 out of 100 cases and that the results become worse the further advanced the case.

The point is to diagnose the cancer and to institute treatment as early as possible.

An operator who does not close his eyes to the extraordinary accomplishment of radiation therapy, must feel strongly impelled to utilize radiation for his operated cases, in order to improve his operative results by combining operation with radiation. My efforts in this direction began in 1913, and I have pursued them since that time, as I believe, with success.

Two methods seem theoretically possible and both have already been practically proved:

1. The preoperative radiation of carcinoma.

2. The postoperative, so-called, prophylactic radiation.

The chief advantage of preoperative radiation lies in the lessening of the primary operative mortality, an advantage which is of the greatest importance for the adherents of the dangerous laparotomy. It is of much less importance for the men who perform the vaginal operation, because this operation has only a very small death rate. A disadvantage of the preoperative radiation, which is admitted by some of its adherents, is that the technic of the operation is more difficult on account of changes in the tissue caused by the rays. Personally, I have had but little experience with the preoperative radiation. In the few cases in which I operated after radiation, I always had to face greater technical difficulties and the only unintended injuries of the ureter in the last fifteen years occurred in those cases which were radiated before the operation. Aside from this there exist no reports of permanent cures in preoperatively radiated cases.

A third, and as I believe, an essential point which speaks against the preoperative radiation is that the primary success of radiation and its apparent result is often so great that the patient becomes free of symptoms, considers herself cured, no longer permits an operation, and in many cases declines any further treatment. That this danger of the too early termination of treatment actually exists and is not merely a theoretical coincidence is shown not only by my experience but admitted by all radiation experts. The momentary successes are so extraordinary that practically a third of the patients withdraw themselves prematurely from the treatment.

These then, are briefly the reasons why I do not practice radiation before operation as a routine measure. Occasionally I radiate cases which seem inoperable and do the operation later when the uterus has become movable. This I have done especially in cases where the microscopic report has shown the existence of still living carcinoma cells in eases seemingly cured by radiation.

On the other hand, I systematically use the second method, the post-

operative, so-called prophylactic, radiation, and I may assert that I was the first who employed radium for postradiation, while a number of others (Gauss) almost at the same time began the prophylactic postradiation with roentgen rays.

I used radium for postradiation for the first time in 1913 in two far advanced cases, which by chance I operated upon on two succeeding days. In both patients I was obliged to cut the parametrium in the middle of the cancer infiltration, so that the operation certainly was not radical. The idea occurred to me during the operation, to apply immediately a radium tube in the place where I had to leave carcinoma. Naturally I thought these two cases lost. To my great astonishment, however, I found both women free of recurrence after three years. As to the definite outcome of both cases I cannot say anything because during the War I lost track of them. Since then, I have worked incessantly on the problem of postoperative radiation. I next radiated only patients in whom I was not sure whether I had operated radically. In 1915 I began to radiate all operated cases with radium and roentgen rays. results of my endeavors are shown in Table II. These results were reached by various methods. First I began with relatively large radium doses about three weeks after operation. The radiation was repeated in intervals of four weeks. The outcome was a noticeable improvement of the results; about 55 per cent of the operated cases remained permanently cured (relative cures) against 42 per cent of those not postoperatively radiated. But we found with this method repeated cases of fistulae. This induced us in the years 1916 and 1917 to make the radium doses smaller. The result was that we saw no fistulae but had a relatively small percentage of permanent cures (44 per cent of operated cases), but better than those operated without radiation. The cause of fistulae and necrosis with my first method was at first incomprehensible to me because I had always used doses far below the dosage applied without injury in the cases we did not operate, but I had forgotten that in nonoperated cases we have a rather thick layer of cervix or carcinoma tissue between the radium and the organs which had to be spared, such as the bladder, the ureter and the rectum, and this layer of tissue acted like a screen and kept the radium at a suitable distance.

It became clear to me that necrosis and fistulae would result more readily if the protective screen were removed by the extirpation of the uterus. Besides I had overlooked a second point, the vaginal stump is poorly nourished and like all scar tissue is exceedingly sensitive to rays, so that already relatively small doses lead to injury. Thus we were in the following situations: If we applied sufficient large doses, we had much better results, but fistulae and necrosis appeared; if we made the dose smaller, we failed to obtain better results than we had accomplished without postradiation. The problem to be solved was: Can a sufficient dose be applied to the desired place without danger of injuring sensitive tissue? The two previously mentioned cases in which I had ap-

plied radium immediately after the operation pointed to the solution of the problem. In these cases the remaining carcinoma tissue was in immediate contact with the introduced radium tube so I was not obliged to use very heavy dosages, because I intended a penetration of few millimeters only. The solution was to apply the radium exactly as I applied it in my first two cases. Since 1917 I have been doing this in the following way: When, after extirpation of the uterus, the peritoneum is closed, I protect the ureters with sterile gauze and insert in each of the parametrial wound cavities 50 mg. of suitably screened radium. The radium remains about six to eight hours. This is the standard method. In cases where I doubt the advisability of being radical with my operation or in cases where there remains suspected infiltrations in the sacrouterine ligaments, a 3 mg. or even a 4 mg. radium tube is laid in the ap-

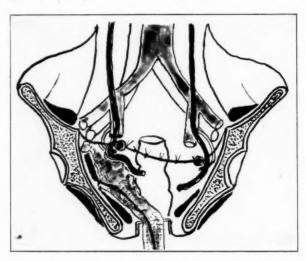


Fig. 1.—Cross section of pelvis showing radium capsule and gauze pack in situ after vaginal hysterectomy.

propriate place. Besides this, beginning two months after the operation, I apply from six to eight prophylactic postoperative cross-fire radiations, placing the radium in the rectum and in the vagina for about three hours. This prophylactic radium application is combined principally with roentgen radiation and in fact usually three series are applied of which the first contains nearly the full carcinoma dose. These series are applied at from three- to six-month intervals.

As far as I know my method of treatment is used at the present time by Knauer in Graz, by Franque in Bonn, by Stöckel in Berlin, and in the Clinic Rosner in Cracow.

Any new method of treatment, if it is worth using, must accomplish two fundamental conditions: First, it must be free from danger and second, it must bring results.

I have used my method in about 400 cases without any complications except transitory rises of temperature. Also from the clinics and sta-

4.25% 8.5 %

tions which are using my method no disagreeable accidents have so far been reported. The second demand which is expected of a new method is that its results are better than that of the one previously in use. In this regard, I am happy to be able to submit the following facts: From the year 1917 until 1920, not all patients were treated according to my method. As it sometimes happens in clinics, what the one assistant recommends is not always approved of by the other assistant and consequently is not done. This occurred also at the Clinic Schauta. If, thus, the number of cases treated according to my method has been less, I am in the agreeable position to make use of very valuable material for comparison.

If I compare the results of the patients treated according to my method with those cases not postradiated, then cases observed after two

TABLE VI. POSTOPERATIVE RADIATION EXTENDS THE LIFE AND INCREASES NUMBER OF PERMANENT CURES

		OPERATED STILL LIVE	NG		
		WITH RADIATION	WITHOUT R	ADIATION	
	+1 year	92.8%	72%		
	+2 years	72.0%	619	%	
	+3 years	61.8%	529	70	
		PERMANE	NT RESULTS		
	+5 years	58.8%	429	%	
RADIATION	Forsell Bowing George	Literature -Heyman g-Fricke Gray Ward	17.45%	23.3% 23.0% 23.6%	(21.8)
OPERATION	Bonney	Literature (abd.) a (vag.)	19.1%	25.0% $22.5%$	
OPERATION + RADIATION	Peham	ne (abd.) (vag.) (vag.) 3rd method	,	28.1% 28.0% 31.8%	
יי	TABLE VIII. ST	ATISTICS OF WILHELM	INENSPITAL, 1	922-1926	
Abs	solute cures			36.4 %	
	Vaginal operati	ion } with Radiatio	n	87.25%	
		with nadiatio	711		

Abdominal operation

Radiation only

years show an increase in relative cures from 72 per cent to 92.8 per cent, and after three years observation from 69 per cent to 72 per cent. These are only temporary cures. What is important in considering the worth of the method, are the permanent cures. My results show that the number of permanent cures (five years or more) increased from 42 per cent to 58.8 per cent. The absolute cure percentage which I obtained with my method is 32 per cent. Comparing these results with the results of laparotomy and with the permanent results of vaginal carcinoma operations with insufficient postradiation, I do not only think myself authorized, but I feel obligated to publish my procedure and to submit it to the profession for trial. Finally I want to say a few words concerning the statistics of cancer treatment in general. We know that with every kind of cancer treatment the application is only local and that cancer very likely is a local disease only in its beginning stages. As long as science has not given us the means to carry out successfully the general treatment of cancer, we must endeavor to make possible on the one hand early diagnosis and treatment, and, on the other hand, to carry out the treatment instituted as energetically as possible.

I have shown and reported the results obtained in carcinoma treatment with the vaginal operation and radiation which is my routine method. But in the treatment of cancer we must not be dogmatic but eclectic and I wish to emphasize that I do not adhere by any means to the vaginal operation in every case. In some cases, however very rarely, I do a laparotomy. But in these cases I likewise insert radium into the parametrial wound cavity immediately after the operation as after the vaginal operation. Finally, I have not operated on other operable cases but only treated them with radiation.

Briefly then, in summary I want to state that we must not adhere to one

method but choose for each case the adequate procedure. Therefore I desire to repeat a request which I made before the Berlin Gynecological Congress ten years ago. We must break off with the old method of gathering statistics. Every gynecologist should take up in his statistics all cases which he sees and all cases in which the patients are living free of recurrence after five years, no matter if they were operated upon by the vaginal operation, the abdominal operation, or treated with radiation only, all these must be considered as permanent cures. In this way one will get a correct picture of the value of the treatment used in different places by different men. If I examine, in this sense, my material from 1920 to 1926, then I arrive at a percentage of 36 per cent absolute cures (five year). This encourages me to adhere to the path I have

taken and to request an examination and trial of the method of treatment

which I have developed.

ENDOMETRIAL TRANSPLANTATION*

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CLINICAL evidence seems to indicate that when endometrial cells are displaced from their usual location, they continue to grow and sometimes produce symptoms. Adenomas occurring in laparotomy scars are ample evidence of this vicarious growth. The method of displacement in these instances is quite definite; namely, operative procedures which include the uterine mucous membrane.

The reasons why this does not occur more frequently and what conditions are necessary when it does occur, are important questions yet to be settled. We do know that normal endometrium is a tissue that possesses a peculiar viability. In addition, it has a marked power of proliferation which we see so well expressed during the changes incident to pregnancy and the rehabilitation of the mucosa following a menstrual period.

The cells of the endometrium are, therefore, in a constant state of change, due to eyelic stimuli. Embryonal cells quickly grow to maturity and are again replaced by a group of new cells of high vitality. Cron and Gey¹ have shown that even the cells of the older endometrium cast off at menstruation can readily be grown in culture media.

The stimuli which produce the rhythmic changes in these structures of the female pelvis are the result of the action of the female sex hormone or hormones, which is being so actively investigated at the present time. Whatever they may be, the fact remains that cell structure in the female pelvis and, particularly the endometrium, is under the control of factors that have much to do with cell growth and vitality.

Numerous investigators^{2, 3, 4, 5} have shown that when endometrial tissue is transplanted in the experimental animal, it retains its power of growth. Sensitiveness to ovarian³ and pregnant⁶ stimuli is maintained. Heterotopic endometrium in the human female displays the same predisposition to shed blood at the menstrual time and produce a decidual reaction during pregnancy.

Sampson⁷ has produced splendid clinical evidence to support his theory of mechanical regurgitation through the fallopian tubes. The supporters of the serosal theory, notably Robert Meyer⁸ and Novak⁹ believe that the preponderance of evidence indicates a metaplasia or heteroplasia of the peritoneum.

^{*}Read before the Central Association of Gynecologists and Obstetricians, Excelsior Springs, Mo., October 10, 1930,

Neither theory adequately explains all of the conditions met with in clinical endometriosis. Much work remains to be done to establish these important questions.

Schochet,¹⁰ in 1916, reported a series of ovarian transplants into the anterior chamber of the eye. He failed to find a metaplasia of the surface epithelium or peritoneum into endometrial-like tissue.

In 1928 Dr. Bauer and I⁶ reported the results of transplanting endometrium from the uterus of rabbits into the anterior chamber of the eye. In this series, we found that endometrial tissue transplanted into this location shows certain definite characteristics, most definite of which was a marked tendency to proliferation with the formation of



Fig. 1.—The course of a blood vessel extending from the iris into the substance of the implant is well shown. The proliferation of typical epithelium outward in both directions from the base of the iris is quite clearly shown.

gland-like spaces. These gland-like structures seemed to have the ability to invade other tissues, such as the iris. We were not able, however, to demonstrate a proliferation of the stromal connective tissue. This seemed to us an important problem, because we find in these islands of heterotopic endometrium in the human a typical connective tissue framework. Are these cells transplanted along with the epithelial elements en masse; are they outgrowths from the original location, or are they local cell reactions to the presence of heterotopic epithelium?

These questions form the basis of this continuation of our previous experiments.

EXPERIMENTAL

We followed the same procedure as we used in our previous work. Small bits of endometrium, ovary and peritoneum were removed and slipped immediately into the anterior chamber of the eye. For comparison, in a few animals endometrium was implanted into one eye and rather large strips of peritoneum or ovary into the opposite eye. Twenty-five rabbits were used; they were killed and autopsied at intervals of from fifteen days to thirteen months. The eyes were enucleated, at once fixed in Mueller's solution and cut in celloidin. Sections were stained with eosin and hemotoxylin to study the extent and type of epithelial proliferation. The connective tissue was stained by Dr. George Bartelmez with the Bielchowsky colloidal silver method to differentiate the stromal reaction from the connective tissue cells of the iris.

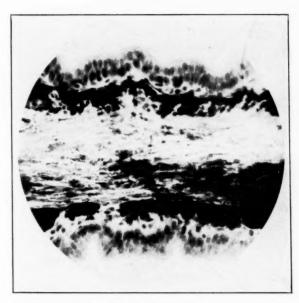


Fig. 2.—The proliferation of epithelium through the pupil onto the under surface of the iris is quite marked in this section. Note the definite subepithelial connective tissue.

RESULTS

Vascularization occurred in the endometrial transplants very rapidly. Occasionally blood vessels could be seen extending toward the implant within twenty-four hours. At the end of three or four days, this was very pronounced and continued so, at least in the larger bits of tissue, until removal of the eye. The alternate blanching and congestion of the implant reported by Schochet and Markee¹¹ was noted several times, but did not seem so marked as they report in the guinea pig. The connections with the vessels of the iris are quite definite. (Fig. 1.)

The epithelium of the implant proliferates outward from the periphery. It often crosses over or through the pupil (Fig. 2), passing over the anterior surface of the iris around the external angle and for varying distances on to the posterior surface of the cornea. These new

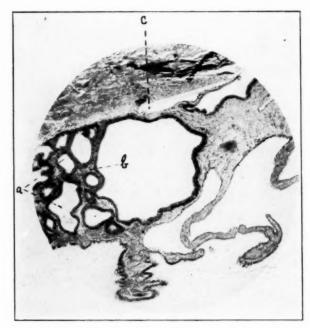


Fig. 3.—In this section a typical group of endometrial-like glands (a) surrounded by an embryonal connective tissue stroma (b) lies deep in the ciliary body. It is separated by normal ciliary tissue from the external angle of the anterior chamber (c).

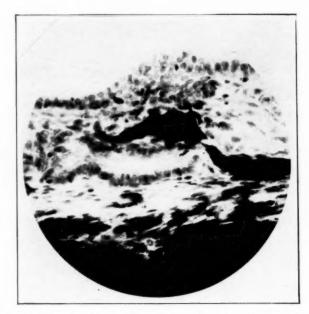


Fig. 4.—The epithelium in this specimen has proliferated downward to produce a gland-like space in the substance of the iris.



Fig. 5.—The typical deposit of silver salts in the epithelium and reticular framework of the body of the implant corresponds to that of the normal endometrium.

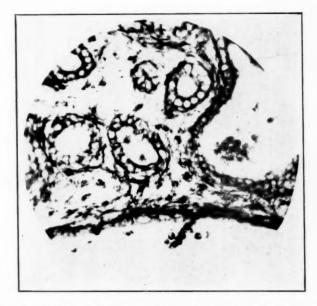


Fig. 6.—Reticular staining in the new connective tissue is not definite. Probably due to the presence of or obscured by the pigment in the iris.

epithelial cells are often ciliated and, in some instances, seem to exhibit secretory activity. This single layer of epithelium is frequently modified to produce gland-like spaces in the angles of the anterior chamber or proliferates downward into the substance of the iris. (Figs. 3 and 4.)

Beneath this layer of new epithelial cells and surrounding these gland-like spaces a stroma of connective tissue appears. This fibrous stroma stained with eosin and hemotoxylin seems definitely different from the connective tissue of adjacent structures. With the Bielchowsky method a thick deposit of silver is formed in this subepithelial connective tissue. We could not however differentiate a characteristic reticulum like we find in the stroma of the implant itself. (Figs. 5 and 6.)

When we attempt to trace these areas of new connective tissue in a continuous layer back to the base of the implant as a source, which we can easily do with the epithelium, we find no connection. It seems

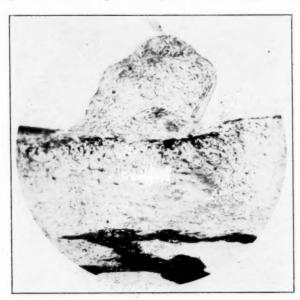


Fig. 7.—The sclerotic bit of tissue left from the implantation of peritoneum. Note the total absence of epithelium both around the implant and on the anterior surface of the iris.

to be only a localized proliferation in widely separated areas. This phenomenon may be the explanation why some areas in human endometriosis are rich in stroma while others are almost entirely epithelial.

We did not find any evidence of proliferation or cell response to foreign tissue in any of the eyes containing peritoneum or ovarian substance. The epithelium of the peritoneum is very difficult to preserve during the necessary manipulations, and may have been destroyed before reaching the site of implantation. The final result revealed a minute sclerotic bit of connective tissue attached to the iris. (Fig. 7.)

The same lack of metaplasia of the germinal or follicular epithelium occurred in spite of actively ovulating ovarian tissue. (Figs. 8 and 9.)

In several instances the proliferated epithelium revealed many characteristics of tubal epithelium; namely, marked ciliation of all cells and the appearance of definite secretion granules. If investigation proves that this does not occur normally in the uterine mucosa of rabbits during the estrus cycle, we may have another avenue opened for the study of those factors causing heteroplasia of cells.



Fig. 8.—A ripening follicle (a) is shown bere deep in the ciliary body. No other epithelial pro ion in present.



Fig. 9.—A higher power magnification of the follicle shown in the previous plate reveals its structure in detail.

CONCLUSIONS

Definite conclusions are hard to draw but we feel that these experiments indicate:

- 1. Uterine epithelium in rabbits possesses more marked proliferative and heteroplastic tendencies than the epithelium of the peritoneum or ovary.
- 2. This proliferative tendency earries with it the property to stimulate a local connective tissue response.
- 3. Transplanted endometrial connective tissue does not tend to proliferate
- 4. Follicular activity is maintained in this location for a considerable length of time.
- 5. Metaplasia of uterine epithelium may be produced by transplantation into the anterior chamber of the eye in rabbits.

This study was only made possible by the kind assistance of Dr. George Bartelmez in staining and interpreting the microscopic slides.

REFERENCES

(1) Cron and Gey: Am. J. Obst. & Gynec. 13: 645, 1927. (2) Hesselberg, Kerwin and Loeb: J. Med. Research pp. 11-33, 1918. (3) Katz and Szene: Ztschr. f. Geburtsh. u. Gynäk. 90: 74, 1926. (4) O'Keefe, C. D., and Crossen, R. J.: J. Missouri M. A. 24: 252, 1927. (5) Jacobson, V. C.: Am. J. Obst. & Gynec. 6: 257, 1923; Arch. Surg. 5: 167, 1922; Arch. Path. & Lab. Med. 1: 169, 1926. (6) Allen, Edward, and Bauer, C. P.: Surg. Gynec. & Obst. 47: 329, 1928. (7) Sampson: Am. J. Obst. & Gynec. 4: 451, 1922; 12: 459, 1926; 10: 462, 1925. (8) Meyer, Robert: Zentralbl. f. Gynäk. 36: 745, 1919. (9) Novak: Am. J. Obst. & Gynec. 12: 484, 1926. (10) Schochet, S. S.: Anat. Rec. 10: 447, 1916. (11) Schochet, S. S.: Am. J. Obst. & Gynec. 17: 328, 1929.

25 East Washington.

Seckinger, D. L., and Snyder, F. F.: Cyclic Changes in the Spontaneous Contractions of the Human Fallopian Tube. Bulletin Johns Hopkins Hospital, 39: 371, 1926.

The cyclic changes in the activity of the muscular wall of the tube closely parallel chronologically the histologic changes occurring in the endometrium and tubal mucosa during the reproductive cycle as follows: During the mid- and late-interval stage, there are rapid contractions showing a marked variation in amplitude. During the premenstrual and menstrual phase, slow contractions of uniform amplitude are found. During pregnancy tubal contractions remain slow and of uniform amplitude.

Comparison with other mammals suggests that in the human the increased activity of the tubal wall during the mid- and late-interval stage is probably coincident with the passing of the ovum through the tube.

No change in the number or activity of the cilia lining the tube was noted at any phase of the reproductive eyele.

C. O. Maland.

PREGNANCY AND LABOR COMPLICATED BY FIBROID TUMORS*

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IN THE time at my disposal I can only touch on certain of the aspects of this rather large subject. In doing so I shall not go into any detailed statistical study but rather try to give you the impressions and conclusions drawn from my own personal observation and experience of cases in which fibroid tumors of the uterus have presented a problem in relation to fertility, pregnancy, labor, and the puerperium.

INFLUENCE OF FIBROIDS ON FERTILITY AND OF FERTILITY OF FIBROIDS

It is very generally accepted that women with fibroid tumors of the uterus are less fertile than those who have none. Graves states that the average percentage of sterility in women in general is 10 to 15 while in women with fibroids it is in the neighborhood of 30 per cent. In the case of the larger tumors the sterility rate is even higher than that.

Women who have had children are less liable to develop fibroids than those who have had none. It is seldom that we find fibroids in the uterus of a woman under twenty-five years of age, and it is rare to find large tumors in a woman who has begun her childbearing before that age and who has had four or five children at two or three year intervals afterward. On the other hand from 30 to 50 per cent of nulliparae at the age of fifty have fibroid tumors. These facts lead to the old question as to whether the fibroids are the cause of the sterility or sterility is the cause of the fibroids. The answer cannot be given until we know something more about the etiology of these tumors. To reason in perhaps a not very scientific way, I am inclined to argue that the uterus is essentially an active organ, its main activity being the embedding, nourishing, and expulsion of the fertilized ovum. If this, its main occupation, is denied it occupies itself in growing fibroids. If a married woman voluntarily prevents pregnancy until she is over thirty or thirty-five or if a woman remains unmarried until after the age of thirty or thirty-five, her chances of having fibroids are greater than if she had had one or more children before that age.

^{*}Read (by invitation) at a meeting of the Brooklyn Gynecological Society, April 3, 1931.

It has been rather a striking fact in my own personal experience with women in the late thirties and early forties who have been sterile for a number of years following marriage and have then become pregnant that a large proportion have fibroid tumors. The most striking example of this occurred last year when I had under my care a patient of forty-seven, childless since her marriage twenty-three years before. She ceased to menstruate and very naturally supposed that she was entering upon the menopause. I saw her after a period of four months' amenorrhea and diagnosed a pregnancy in a uterus containing several large fibroids, so that the uterus at this time reached well above the umbilicus. She went to term and was delivered of a healthy child by cesarean hysterectomy. In the past four years I have had seven other patients with fibroid tumors, all over thirty-five years of age when their first pregnancy occurred and all of them sterile for over seven years.

INCIDENCE OF FIBROIDS IN PREGNANT WOMEN

Two previous reports have been made on the incidence of fibroids in pregnant women in the Sloane Hospital. Craigin and Ryder in 20,000 cases found 89 or 0.45 per cent. Pierson in 30,856 cases found 250 or 0.8 per cent. In the 11,675 patients delivered in the hospital from the date of Pierson's report to the end of February, 1931, fibroids were noted in 157, an incidence of 1.3 per cent. The steadily rising incidence figure is probably due to more accurate reporting for many of the tumors in our present series were extremely small and were of no clinical importance. In forty of the 150 cases the diagnosis might very well be regarded as doubtful. We may take it then that the incidence of significant fibroid tumors in pregnancy appears to be round one per cent. This bears out the belief that fibroid tumors are a cause of sterility as the incidence in a similar age group of all women would show a higher percentage of tumors. The average age of those patients who had significant fibroids was thirty-three.

In addition to causing sterility fibroid tumors are apt to lead to abortion, miscarriage, and premature labor. There is a history of 71 early and late abortions in our 157 patients. This is above the average for women in general. There were also 24 premature labors which again is a high figure. These numbers are in accord with other statistics quoted by Pierson in which the abortion and premature labor rate ranges from 15 to 24 per cent.

When an otherwise normal woman with a fibroid tumor in her uterus remains sterile or has one or more abortions it is a fair assumption that the fibroid is the cause of her disability. In such cases a myomectomy should be advised. One of the great advances in gynecology in the past ten years is the increasing number of myomectomies which are being performed in preference to hysterectomies. It

is possible to enucleate even large tumors and leave a functioning uterus. With proper closure of the beds of the tumors the uterine wall should be as strong as ever it was and such of these patients as subsequently become pregnant should be able to deliver per vaginam. I do not know if it is the experience of others but I have noticed several times that the first pregnancy following a myomectomy not infrequently terminates in abortion. I have observed the same thing in patients on whom a suspension of the uterus has been done for retroversion causing sterility or abortion. In both conditions subsequent pregnancies usually proceed normally. So much have I been struck by those facts that I warn patients not to be disappointed if the first pregnancy after operation terminates prematurely. At least one year should elapse between operation and the beginning of a pregnancy. The following case illustrates the point:

Mrs. W., aged thirty-six. Married for three years, no pregnancy. For past four years menstruation more profuse than before. Examination showed a retroverted uterus containing a fibroid tumor the size of an orange in the uterine wall. Myomectomy recommended but operation not consented to until a year and one-half later by which time the tumor was considerably larger. At operation a large interstitial fibroid was enucleated together with five smaller ones, the largest of which was the size of a walnut. Convalescence was uninterrupted. Ten months later she became pregnant, had a missed abortion at the second month and was curetted at the end of the third month. In this case no further pregnancy has occurred so far.

THE COURSE OF PREGNANCY IN A UTERUS WITH FIBROID TUMORS

Abortion and premature labor have been referred to. In a large number of cases in which the fibroid or fibroids are small the patient experiences no disability whatever. Such tumors may only become apparent in the third trimester and when situated in the anterior wall may be more easily palpable toward full term. The reason for this is that small interstitial and subserous nodules tend to be projected as distinct knobs as the uterus distends and its wall thins out. This is the factor which makes myomectomy such an easy procedure when done at the time of a cesarean section or in the course of pregnancy. On the other hand large multiple tumors may become less defined and less easily palpable toward term owing to the general softening of the uterus. I have often been surprised at the large size of tumors at the time of cesarean section in patients whom I had not seen in the earlier months. Such observations have encouraged me in cases seen early to advise the continuance of pregnancy even when the tumors were large and when it seemed hardly possible that the abdomen could accommodate them and a full-term pregnancy as well. The patient may have more discomfort than ordinarily experienced toward term but in the absence of complications has, in my experience, been able to continue the pregnancy to term or so near to it that a strong child was assured. It is truly astounding how in such cases the abdomen manages to accommodate the large bulk of child plus tumor.

Some apprehension may be felt as to whether the presence of these large tumors may cause some fetal deformity or may favor such a complication as placenta previa. In our present series of 157 cases there was one child with clubfoot and one case of placenta previa. It is now established that fetal deformity is practically always developmental and not environmental in origin.

The complication most often encountered during pregnancy is necrobiosis or red degeneration. It was present in 23 out of 41 patients in whom hysterectomy or myomectomy was done. It is a complication which may occur in a fibroid tumor at any time but is especially common during pregnancy and in the puerperium. It is a vascular lesion resulting from interference with the blood supply to the tumor. There is extravasation of blood and deposit of blood pigment so that the tumor becomes red in color, resembling a raw beefsteak on section. The tumor cells die so that on section all nuclear staining is lost and only the outlines of the cell bodies remain. In other words it is an infarction. Later the tumor becomes dull grey in color and it may break down and liquefy. As a rule it remains sterile but secondary organismal invasion from the uterine cavity or from intestinal adhesions may occur. Apparently it takes several months for gross breaking down of the tumor to occur. It is frequently seen at term when from the symptoms it is known that the complication began early in pregnancy. These symptoms are pain at the site of the tumor in the uterine wall, tenderness which may amount to acute pain on palpation, and temperature which seldom exceeds 100° or 101°, except in secondarily infected cases. Pain and tenderness, together with some rise in temperature, are practically pathognomonic of red degeneration of a fibroid in either the pregnant or the nonpregnant uterus. Ten years ago operative interference was regarded as necessary whenever those symptoms appeared. Increased experience has shown that even when they appear fairly early in pregnancy it is usually possible to carry the patient along to term or at any rate to the period of viability when operation can be undertaken with the hope of a living child. In a certain number of cases operative interference may be imperative earlier in pregnancy.

Let me cite one or two cases to illustrate these points:

Case 1.—Mrs. B., aged thirty-eight; married for seven years. No pregnancies until the present one. Was told six years before that she had uterine fibroids. Seen by me when she had missed one menstrual period. At this time irregular tumor masses could be felt reaching to the umbilicus and it was impossible to diagnose pregnancy with certainty. There was considerable tenderness over the largest of the tumor masses, and the patient had had a good deal of pain three weeks previously but this was now less severe. As the pregnancy progressed the pain and tenderness diminished. The note made at the fifth month says, "Uterus is ac-

commodating itself very well to the abdomen.' At the end of the sixth month it is noted that "the tumors feel softer" and at the end of the seventh month my record states that "fibroids cannot now be distinguished from the rest of the uterus except one felt through the vaginal fornix which displaces the cervix to the left." Cesarean hysterectomy was performed two weeks short of term. The largest tumor showed liquefaction secondary to a red degeneration, the surrounding tissue being grey in appearance.

Case 2.—Mrs. M., aged thirty-five. Married eight years. At age of twenty-nine had a myomectomy and suspension of uterus. First seen by me in the sixth month of her first pregnancy. At this time the uterus reached almost to the costal margin and several hard nodules as big as apples could be felt in the wall. There was also one to be felt in the lower uterine segment, displacing the cervix well away from the midline of the pelvis. For ten days patient had had sharp pain in the abdomen and one of the tumors on the left side was very tender to touch. Pain and tenderness lasted for about two weeks and then subsided. Patient went to term. Cesarean section was performed and, owing to the multiplicity of the tumors, was followed by supravaginal hysterectomy. Examination of the tumors showed the one on the left side to be liquefied in the center, the surrounding tissue being pale grey in appearance.

The next cases also showed red degeneration but the symptoms were much more severe. Patient was carried, however, to the period of viability and a healthy child delivered by cesarean section followed by myomectomy.

Case 3.—Mrs. Z., aged thirty-four. Gravid i. Para o. First seen by me when three months pregnant. At that time a firm, solid mass could be felt reaching to umbilicus to the left of midline and a smaller one to the right. Cervix and lower uterine segment soft. At the fifth month pain and tenderness appeared in the tumor on the left. This persisted in varying degree until term. From time to time she had to remain in bed for one or two days. Cesarean section was performed within two weeks of term, four fibroids enucleated from the wall. The largest, that on the left side, was dull grey in color, and was liquefied in its center.

Case 4.—Mrs. II., aged thirty-nine. Married for fourteen months. First seen in the fourth month of her first pregnancy when several large fibroids were detected, one of them in the posterior culdesac and fixed in the pelvis. She complained of dull pain in the lower abdomen with acute exacerbations from time to time. She was extremely anxious to have a child and readily consented to hospitalization. She remained in the hospital for four months. She had practically continuous pain, at times so severe as to necessitate various sedatives and hypnotics. The tumors in the abdomen and pelvis were tender throughout. There were occasional rises in temperature but it never went over 100°. Cesarean hysterectomy was performed at the end of the eighth month. Child well developed and healthy. All of the tumors showed red degeneration, the pelvic one having a large cavity in its center filled with dark syrupy fluid.

It is not always possible to postpone operation until near term. In the case which follows I was mistaken in my diagnosis but even had a correct diagnosis been made I doubt if any other procedure would have been justified.

Case 5.—Mrs. K., aged twenty-six. Seen by me in consultation when she was four and one-half months pregnant on account of severe lower abdominal pain, vomiting,

and retention of urine. Her doctor had made a diagnosis of retroflexed gravid uterus. Examination showed the uterus in the abdomen and a round, very tender swelling filling up the pouch of Douglas and pushing the cervix above the pubes. I made a diagnosis of incarcerated ovarian tumor with twisted pedicle. On opening the abdomen the swelling was found to be an intramural fibroid the size of a large orange growing from low down on the posterior uterine wall. Myomectomy was done and the bed of the tumor closed. She miscarried twenty-four hours later. The tumor showed acute red degeneration. Two years subsequently she had a normal delivery.

In the following case hysterectomy was deemed wise at the fourth month.

CASE 6 .- Mrs. S., aged forty. Colored. Married for twenty years but never pregnant until the present time. She was seen in the gynecologic clinic January 20, 1931, and gave a history of having had her last menstrual period in October, 1930. Shortly after missing her November period she began to have severe pain in the left side of the abdomen and had "chills and fever." Pain continued and she began to lose weight. When first seen in January, 1931, after three months' amenorrhea a mass could be felt in the abdomen reaching well above the umbilicus. It was irregular in outline and tender on palpation. The softened cervix and lower uterine segment together with a positive Aschheim-Zondek test established the diagnosis of pregnancy. She was seen from time to time in the clinic but as pain continued she was admitted to the hospital for observation and treatment. During the following ten days pain and tenderness increased, and as she was not at all anxious to have a child and could not promise cooperation by prolonged hospitalization it was deemed wise to operate immediately. The uterus contained several large fibroids, all interstitial, so subtotal hysterectomy was done leaving both tubes and ovaries. The tumors all showed red degeneration, the larger ones being broken down and liquefied in the center.

Let me mention and illustrate with a case, a much rarer acute complication which may necessitate immediate operation, viz., torsion of the pedicle of the tumor.

Case 7.—Mrs. U., aged thirty-five. Married for two years before she became pregnant in July, 1930. Seen by me when three months pregnant at which time the uterus plus fibroids reached to above the umbilicus. Several distinct large tumors could be outlined, the largest about the size of a grapefruit. She progressed normally until the fourth month when she had a severe attack of abdominal pain with vomiting. She was brought into the city four days later, pain and vomiting having continued. Pulse was rapid and she was dehydrated. The abdomen was distended and the tumor on the right side exquisitely tender. On opening the abdomen a pedunculated tumor presented. Its pedicle had a twist of 360 degrees and the tumor was dark in color. As there were other large fibroids present it was deemed wise to do a supravaginal hysterectomy.

EFFECTS OF FIBROIDS ON LABOR

That fibroids complicate labor is evident from the following statistics of our 157 cases. In those there were 71 operative and breech deliveries, making 48 per cent of the total. These included 23 forceps extractions, 4 versions, 35 cesarean sections, and 9 breeches. Of the 35 cesarean sections only 15 were performed primarily because of the fibroids. In the other 20 the operation was done on some other indica-

tion and the fibroids, usually small ones, were discovered after the abdomen was opened.

There were two intrauterine fetal deaths and 18 stillbirths.

Adherent placenta was encountered only twice. Both patients had small submucous tumors and both had had several abortions.

Postpartum hemorrhage occurred in three cases. In none of them was it severe. As mentioned before there was one case of placenta previa.

There were four maternal deaths but in only one could the death be ascribed to the fibroid complication. This patient had large fibroids; she had several fainting spells during her pregnancy and had a very variable blood pressure. A cesarean hysterectomy was performed and she died three hours thereafter of cardiac failure. The abdominal wound was reopened on the chance that there might be a hemorrhage from a slipped ligature but none was found. The condition of the myocardium in women with large fibroids should always be taken into account. If there is evidence of impairment of function and the patient is pregnant it may be better to perform hysterectomy early rather than let the pregnancy continue.

The other three deaths were due to (1) tuberculosis of the kidneys; (2) pneumonia following cesarean section done for flat pelvis, the fibroids being unimportant and (3) chronic cardiac valvular disease in a patient who had cesarean section performed because of this and because of a contracted pelvis, the fibroids being unimportant.

It is evident from this recital that fibroid tumors of appreciable size whether multiple or single are a serious complication of pregnancy and labor. But if each individual case is carefully studied and the proper line of treatment mapped out and properly executed a favorable outcome to mother and child can usually be assured. It should be explained to the patient as early as possible that if the pregnancy is to continue she may require to spend a considerable part of the time in bed and that she may have some pain. If she is unwilling or unable to face these possibilities or if it is evident at any time during the pregnancy that degenerative processes are progressing very rapidly or that the myocardium is showing signs of impairment immediate hysterectomy or myomectomy should be advised.

It is advocated by some obstetricians and gynecologists that myomectomy should be performed early in pregnancy in all cases and some go so far as to empty the uterus from below before performing it. I cannot subscribe to this method. The pregnancy in progress may be the only pregnancy the patient may have, especially if she is elderly. A myomectomy during pregnancy is very likely to cause abortion. In this series of cases there were three myomectomies done during pregnancy; one, which aborted in twenty-four hours, has already been mentioned. A second was performed at the sixth month on a mis-

taken diagnosis of twisted ovarian cyst. On opening the abdomen a soft, fluctuant fibroid, the size of a fetal head, was found attached to the fundus by a pedicle of three inch diameter. Another smaller, more sessile tumor was situated lower down and a few seedling tumors were present in other parts of the wall. In removing the larger tumor considerable hemorrhage was encountered which owing to the tenseness of the uterine wall could not be controlled by suture. Rather than sacrifice the uterus it was, therefore, determined to perform hysterotomy. The fetus and placenta were removed when it was found that the larger tumor was over the placental site. With the emptying of the uterus the bleeding was easily controlled and the other tumors were enucleated. Both the large tumors showed red degeneration and necrosis, the wall of the largest one being a mere shell enclosing fluid contents. This patient had a normal delivery fourteen months later. The third case of myomectomy was one in which in the course of an operation for appendicitis in a woman in the third month of pregnancy two small subserous fibroids were found in the uterine wall and removed. She delivered normally at term.

A myomectomy or a hysterectomy can be performed at any time during a pregnancy if some acute complication renders such procedure necessary. Such interference should be withheld until the emergency arises. Myomectomy at the time of cesarean section is usually an easy procedure. When the shelling out of the tumor is done carefully there is not excessive bleeding. Cervical and intraligamentous tumors may be more easily dealt with then than at any other time. It is my rule to perform either myomectomy or hysterectomy at the same time as a cesarean section when the latter has been undertaken because of the fibroids. So far I have not had the courage to leave a uterus containing large fibroids on the chance of a succeeding pregnancy and another cesarean section.

A subconscious love of the dramatic may have led me to place too much emphasis on the operative side of this subject and I must take care that I do not convey the impression that operative interference is necessary in the majority of cases where fibroids complicate pregnancy. Small fibroids even when several are present in the uterine wall have little effect on labor. Subserous nodules are more easily palpable during contractions and may be distinctly tender. In such cases labor usually progresses normally. When there are several tumors of the larger type uterine contractions are adversely affected, they are less powerful and less effective than normal, both in the first and second stages. For this reason if the patient is a primigravida over thirty-five years of age the safest method of delivery may be by cesarean section. In younger women and in multiparae if there is no tumor obstructing the pelvic canal and there is no evidence of red degeneration, the patients may be given a trial of labor, operation

being resorted to only when it becomes evident that only very slow progress in the first stage is being made. If one of the tumors is actually in the pelvis displacing the cervix or obstructing the canal cesarean section is usually imperative. It is sometimes found, however, that a tumor growing from the lower uterine segment and definitely in the pelvis at the end of pregnancy is pulled up during the first stage of labor so permitting delivery per vaginam. In the case of pedunculated tumors it may be possible to push them above the pelvic brim at the time of labor. The following cases are illustrative of this:

Mrs. H., aged twenty-eight, para i. One pregnancy four years before. Seen for first time when four months pregnant when a fibroid tumor the size of a large orange could be felt in the left side low down in the uterine wall. Patient was hospitalized twice during her pregnancy on account of pain in the tumor and pyelitis. At term she went into spontaneous labor. The head was high above the brim until the end of the first stage. The fibroid, meantime, had risen well above the brim. The head then entered the pelvis and the patient had a spontaneous delivery of a healthy child, the whole labor lasting nine hours. This patient now three months postpartum is to enter the hospital soon for myomectomy. The tumor is now painless and is not tender.

Mrs. C., aged thirty, para ii. Last pregnancy four years ago. At the onset of labor it was found that there was a firm rounded swelling, the size of an orange, in the posterior culdesac. With two fingers in the rectum this could be pushed above the pelvic brim allowing the head to enter. An easy midforceps extraction was done, the whole labor occupying seven hours. Patient ran a temperature for the first six days of the puerperium with considerable lower abdominal pain. The pelvic tumor was easily palpable in the pouch of Douglas on her discharge. Six months later the tumor was removed. It was a pedicled fibroid with red degeneration.

When a patient with uterine fibroids has delivered from below there is a liability of red degeneration developing during the puerperium or, having begun during pregnancy, progressing postpartum. When symptoms are acute with marked pain and tenderness immediate myomectomy or hysterectomy should be performed. In our present series of cases there were 7 in which hysterectomy was performed subsequent to delivery, the earliest being done two months postpartum.

ATROPHY AND DISAPPEARANCE OF TUMORS AFTER LABOR

It is commonly stated in our textbooks that fibroids tend to atrophy and may entirely disappear after pregnancy and labor. In our records there are several cases in which it is noted that small tumors diagnosed during pregnancy were undetectable in the postpartum follow-up clinic. We have no record of a tumor of moderate size disappearing, and it is a very difficult thing to be certain of diminution in size. I wonder if some of the cases of disappearance of the larger tumors are possibly cases of red degeneration with liquefaction and absorption. That moderate sized tumors may diminish very materially

in size or even disappear seems to be an undisputed clinical fact but I have not personally observed it.

To sum up it may be stated that while fibroid tumors may constitute a major complication of pregnancy, labor and the puerperium, the smaller tumors usually permit the patient to proceed to term and deliver normally or with ordinary obstetric assistance. Every patient with fibroids of significant size requires careful watching and guiding during her pregnancy. The most frequent complication during pregnancy is red degeneration. While in some instances symptoms of this may be so acute as to necessitate surgical intervention in the course of the pregnancy, in the majority of cases the patient can be carried to term and delivered by cesarean section followed by myomectomy or hysterectomy. Or she may be delivered per vaginam and a subsequent myomectomy or hysterectomy be done. The size of the tumor may necessitate removal before term but in the absence of acute symptoms time should be given to see whether the abdomen will not accommodate it. (For discussion, see page 445.)

THE TREATMENT OF OCCIPITOPOSTERIOR POSITIONS WITH ESPECIAL REFERENCE TO MANUAL ROTATION*

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THE management of occipitoposterior positions has been the subject of a voluminous literature. My only reason for adding to the already large amount of material which exists is the desire briefly to discuss the procedure which has been of very great assistance to my associates and myself in the Evanston Hospital.

While it is true that today obliquely posterior positions are not regarded as seriously as they were they still occasion some anxiety. Varying methods of dealing with them have been proposed and used, in some instances with great satisfaction, by various writers. It is probable that some of the dread which posterior position occasions is, as Williams suggests, due to the fact that many posterior positions are unrecognized and anterior rotation takes place without the attendant's knowledge and delivery follows normally. Many of those which terminate favorably are therefore not recognized as posterior positions and only those in which deep transverse arrest or posterior rotation occurs are diagnosticated as posterior positions. That this is possible is apparent to any obstetrician of experience for cases are occasion-

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ally seen in consultation in which women have been long in labor with a posterior position of which the attendant has been quite unaware.

I have taken as a basis for this report the cases of occipitoposterior position occurring in my own private practice in the past six years. These number 285 out of a total of 1,131 private cases. Posterior positions were therefore 25.1 per cent of this number and included 256 R.O.P. and 29 L.O.P. presentations.

As I desire to discuss a maneuver in which I am particularly interested it seemed better to make use of a series of personally managed cases rather than to include the entire hospital material. In all cases the general physical condition of the woman was known and pelvimetry had been done.

It is well known among obstetricians that the first stage of labor in the presence of a posterior position may be longer than is the case with anterior position. Precisely why this should be so is not easily explained but the fact is recognized.

Good obstetric strategy demands that the woman should be gotten into the second stage with her physical powers as nearly intact as may be and with the least possible impairment of her nervous forces. To this end the judicious employment of some form of opiate is often of great value. With sufficient relief of pain the majority of women who have long labors may be carried through the first stage without serious exhaustion. A greatly exhausted woman is more likely to become infected than one who is not. The exhausted woman is also more likely to bleed severely. The management of occipitoposterior positions may with entire propriety be said to begin in the first stage.

Dilatation should occur by the normal mechanism and any interference to hasten it should be avoided unless excellent reasons exist for doing something. Occasionally, when the last portion of dilatation is long in occurring, and it is feared that too great prolongation of the labor will result in bringing the woman into the second stage in a condition of too great fatigue, dilatation may be completed manually or by Dührssen's incisions. These cases should be chosen carefully after deliberate weighing of all factors. They are not frequent. The bag of waters should be preserved intact if possible until dilatation is complete or nearly so. Should rupture occur early in labor the recumbent position may assist in preserving at least some of the fluid in the uterus.

After complete dilatation has been attained voluntary effort on the part of the woman may begin. If any suspicion of disproportion exists it must now soon be decided whether it is present or not. The suggestion that the woman be caused to lie upon the side to which the occiput points has been made by various writers for many years. It should be treated with the respect due to age but my own experience leads me to believe that it is of little value. Apparently Williams has

arrived at the same conclusion. It is probable that in most instances the head enters the pelvis in the transverse diameter and turns toward the front or the back, most frequently the former, after passing the inlet. If the occiput turns backward, or if the head enters the pelvis with the occiput obliquely posterior, a posterior position results. As the head descends the most dependent portion, which, in the well flexed head is the occiput, tends to rotate to the front after striking the pelvic floor. Thus a partially deflexed head is rather more apt to rotate posteriorly.

After dilatation is complete and the labor has entered the second stage the accessory forces of labor, or voluntary effort on the part of the mother, may be brought into play. This should be carefully abstained from until this time. The observant obstetrician will note by rectal examination whether, as dilatation becomes complete, a bit of cervix becomes caught between the head and the symphysis. This is more likely to happen in posterior positions as the head does not fit as well into the cervical ring. If this occurs it may delay the labor considerably and, as time goes on, it becomes edematous and thick and is less easy to deal with. It should be gently pushed upward by the fingers during a pain when, but not before, the cervix is otherwise entirely gone. If the incarceration of the anterior cervical lip between the head and the symphysis is allowed to remain unrelieved the anterior portion of the cervix may be pushed downward by the advancing head. This produces a strain on the anterior vaginal wall and is a potent cause of cystocele. Its relief assists the progress of labor, in some cases considerably.

It is with the cases which do not progress so favorably that I am particularly concerned at present. There are a considerable number of cases in which some form of operative assistance is needed. While hastiness in proceeding to operative measures is not wise, it is not to be forgotten that unreasonable prolongation of the second stage may have serious consequences. Among these the development of a contraction ring may be mentioned and emphasized.

Under some form of pain relief, the best at this stage of labor being gas and oxygen analgesia, labor is allowed to continue. The pains are often less effective than in anterior positions and the head tends to lie higher. It is hoped that the head may be caused to descend through the pelvis upon the perineum, and to rotate anteriorly. Should this occur spontaneous delivery or an outlet forceps terminates the delivery. This occurred in 65.4 per cent of this series of cases.

Should failure of anterior rotation occur, or should the head rotate anteriorly only part way and come to rest in the transverse position, the aid of art becomes necessary. Various methods of dealing with this situation have been suggested. Some obstetricians prefer rotation with forceps while others believe that version should be used in

a far larger proportion of cases than it has been in most clinics heretofore.

In our own work we have found very useful a method of manual rotation differing somewhat from those usually described but resembling most closely the maneuver suggested many years ago by Tarnier. After waiting for the head to become engaged and for any necessary moulding to occur, and this is essential to success, the right hand is introduced and the head grasped with the fingers and thumb which are spread out as much as possible in order that such force as may be

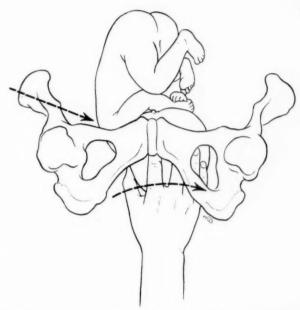


Fig. 1.—Manual rotation. Head grasped by whole hand (right) and rotated to anterior position. The left hand (upper arrow) pushes the shoulder toward the woman's left, aiding the rotation.

used shall be distributed as widely as possible over the fetal head. At the same time the left hand is applied to the mother's right lower flank, as nearly as possible under the fetal shoulder. Simultaneously the hand within the vagina grasping the head, and the external hand, rotate the head and body to the mother's left. For success in this maneuver it is necessary that the uterine musculature be relaxed with ether. Gas anesthesia may be resumed, if desired, as soon as rotation has been accomplished.

It is advisable to overcorrect the head if possible, that is, to continue the rotation until the occiput has just passed the median line. The thumb of the internal (right) hand is then withdrawn, the tips of the fingers being left in contact with the lower part of the child's face in order to prevent backward rotation into the original position. At this point the operator's left hand leaves the abdomen of the

mother and is replaced by the hand of an assistant or nurse. This replacing hand may be applied under the sterile sheets without disturbing asepsis. The left blade of the forceps is then introduced by the operator with his left hand, passing the blade inside the fingers of the right hand which still remains in place. After this blade is introduced an assistant holds the handle, at the same time exerting gentle traction laterally. This causes a gentle lever action to be produced, the blade of the forceps causing pressure against the child's face in place of the operator's hand, thus hindering backward rotation. The

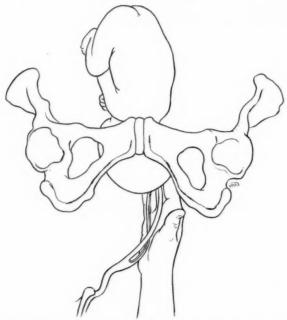


Fig. 2.—Anterior rotation complete. Right hand maintains head in anterior position while left blade of forceps is applied.

right blade is then introduced and the blades closed. With one or two fingers the operator assures himself that the occiput remains anterior. Extraction may now be done.

Should the position be a left occiput posterior a similar procedure is carried out, again using the right hand. The internal part of the rotation is done in a similar manner though in the opposite direction and after rotation has been accomplished it is usually best to make pressure with the fingers of the internal hand against the lateral aspect of the occiput rather than the lower part of the face in order to prevent backward rotation into the left posterior position. The external manipulation is done by using the left hand, the operator reaching across the mother's lower abdomen and trying to hook the fingers under the shoulder on her left side, and pulling rather than pushing as the internal rotation goes on. The forceps application is the same.

If possible the rotation is done without pushing the head upward. If this is impossible one need not hesitate to disengage the head, as, any necessary moulding having occurred, it will reenter the pelvis. It should be emphasized again that this maneuver is not to be carried out until the head is well into the pelvis and moulding, if necessary, has occurred. The inexperienced obstetrician should beware lest the apparent descent of a markedly moulded head, and this impression may be increased by the presence of a caput succedaneum, may cause him to assume that the head is much deeper in the pelvis than it really is. An error of this sort may lead to unexpected operative difficulties.

Disengagement of the head must of course only be done when success is impossible without it. When it is necessary, the operator must always be on the lookout for the possible prolapse of the cord. This occurred once in the series which forms the basis of this paper. Immediate version and extraction was done and the child lived.

If the head is not engaged, and it appears necessary to intervene, version should be chosen instead of manual rotation and forceps unless cesarean section is indicated.

TABLE I.—SPONTANEOUS OR FORCEPS DELIVERIES

Total Number	285	
Spontaneous rotation and delivery	83	29.1%
Spontaneous rotation and forceps	104	36.3%
Manual rotation and forceps	76	26.6%

The procedure described above has been done in 76 cases of the series which forms the basis of this report. It was attempted and failed of success in 9 cases. In these cases version was done at once. In 8 other cases version was done without any attempt to do a manual rotation. Simple outlet forceps after spontaneous rotation was done 104 times.

No maternal death occurred. As to morbidity, any woman whose temperature rose to 100.4° at any time was included in the morbidity list. This occurred in 10 cases after manual rotation, or 15.1 per cent. This is a severe standard by which to judge and gives a higher morbidity rate than the more lenient standards which are ordinarily used. There were seven versions (41.1 per cent) and 18 spontaneous or low forceps deliveries (11.3 per cent) with fever.

In this series only one fetal death occurred. This was a premature baby, delivered spontaneously after a rapid labor at seven months' gestation. There were no infants injured.

We prefer the method of manual rotation and forceps to forceps rotation for the following reasons:

1. By using the hand the operator is able at all times to know whether the head is responding to manipulation or not.

2. Should the first grip of the head be imperfect, and should the operator feel the skull giving or bending under his fingers, the grip can be altered or shifted a little to prevent this.

3. If rotation is not easily accomplished at the level at which the head is found, the head may easily be shifted upward, or disengaged if necessary. If disengagement is found necessary, prolapse of the cord must be watched for.

4. There is a notable freedom from the deep upper vaginal tears which are rather likely to occur in forceps rotation.

5. By the method described, only the right hand is used, regardless of the side upon which the occiput lies. This permits the introduction of the left blade of the forceps first in all cases and obviates the awkward readjustment of the handles of the instrument when the right blade is introduced first. It reduces intravaginal manipulation to a minimum. The use of tenacula or other instruments to hold the occiput in the anterior position is unnecessary. The assistance of the external hand is of great value.

It should be emphasized that the following conditions, in addition to those usually given in standard textbooks for forceps, should obtain before proceeding to manual rotation and forceps:

1. The head must be engaged. If moulding is necessary this must already have occurred.

2. The second stage should not have been allowed to proceed so long that a contraction ring has formed.

3. Ether anesthesia is requisite for the production of relaxation of the uterine musculature. With the lesser degree of relaxation accompanying gas anesthesia, success is much more difficult of attainment. The administration of ether may be preceded and followed by ethylene or nitrous oxide, so that the duration of ether anesthesia may be only a matter of a few minutes. After rotation is accomplished we return to ethylene.

CONCLUSION

This maneuver has been in use in our maternity for a number of years. Since becoming accustomed to it we have ceased to regard the posterior occipital position with dread, as we feel that in nearly all cases, should anterior rotation fail to occur spontaneously, we can deal with the situation successfully. We have been pleased with the absence of infant mortality and of severe maternal injury. While the method requires a certain amount of dexterity it seems that the results which may be attained by its use will well repay the trouble expended in its acquisition.

636 CHURCH STREET.

(For discussion, see page 450.)

PUERPERAL GANGRENE OF THE EXTREMITIES*

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A LTHOUGH puerperal gangrene of the extremities has been discussed a number of times in the literature, its rarity justifies the addition of another case to the relatively few already reported.

In 1916, Stein reported two cases and reviewed the literature up to that time, when 71 cases had been reported in the puerperium, and five after gynecologic operations. In 1925, he again reviewed the literature and discussed 10 cases, reported since his last article. Four of these followed operations and 6 were in the puerperium, making a total of 77 cases of gangrene following abortion or labor. Since 1925, reports have been made of 22 cases in the puerperium, making a total of 99 cases, or with the present one, 100. We add this to Stein's table, which was published in 1925.

	UP TO 1916	1916-1925	SINCE 1925	TOTAL
Puerperal Gangrene				
(Lower Extremities)	53	4	15	72
Gangrene after Abortion				
(Lower Extremities)	3	1	8	12
Puerperal Gangrene				
(Upper Extremities)	10	1	0	11
Gangrene after Abortion				
(Upper Extremities)	1	0	0	1
Gangrene During Pregnancy	4	0	0	4
0 0 .		-	_	
Total	71	6	23	100

The etiology of the condition has been fully discussed by Stein in both his articles, but it is mentioned again, because of the 17 cases in the German literature since 1925. Gynergen or other ergot preparations are mentioned as etiologic factors in 12 of them. In all the cases but one, fever or other evidence of infection was present.

This was Kienlin's case, which had thrombosis of both femoral veins and angioneurotic edema. Newmann's patient had "septic endometritis," but examination of the amputated leg showed no thrombi or emboli, only marked contraction of the arteries. Moskovitz states that his case showed definite signs of ergot poisoning, also a puerperal infection, and the gangrenous lesion was similar to that in our case, which received no ergot. It is impossible, of course, to say that the ergot was not the cause in these cases, but the presence of infection, plus the rarity of ergot poisoning, make it somewhat questionable, hence they are included.

^{*}Read before the St. Louis Gynecological Society, March 13, 1931.

Infection is the one etiologic factor present in all cases and results in vessel obliteration and gangrene. Stein's classification brings this out.

The case here reported is particularly interesting since it is the only one following cesarean section. Other unusual features are the type of pelvic deformity, the development of infection after a Porro operation in a clean case, and the isolation of anaerobic streptococci from metastatic abscesses.

The patient was forty-two years of age, and had had two previous sections seven and six years ago on account of narrow pelvis. Complete x-ray studies of all the bones showed osteitis deformans involving pelvis, upper halves of both femurs,



Fig. 1 .- X-ray of pelvis.

spine, right humerus, left fourth metacarpal, frontal and parietal bones. The pelvic deformity, as seen in the illustration, is a marked narrowing of the inlet. The only complication during pregnancy was an increasing edema of both feet and legs during the last two months. The patient entered the hospital at term, in labor. At this time the edema was extreme. One vaginal examination was made. Cesarean section with supravaginal hysterectomy was done with considerable difficulty, owing to adhesions from previous operations. An adherent loop of intestine at the upper end of the incision was cut and not noticed until closure. This was repaired. The patient left the operating room in poor condition and steadily became worse in spite of intravenous glucose, etc. Two and one-half hours after the operation, the blood pressure dropped to 58 systolic, when the patient was transfused, following which her condition was satisfactory. No signs of peritonitis developed, but a mass appeared in the right lower quadrant the size of a grapefruit, which was slowly absorbed. This was evidently a hematoma and may have been responsible for her shock. The day following the operation, the temperature rose

to 39.5° C., and remained between this point and 38° for thirty-two days. It then remained below 38° for sixteen days and subsequently rose to between 38° and 39°, returning to normal 60 days postoperative. The first rise was due to the gangrene and abscesses of the leg, and the second, to the abscess of the thigh.

On the fourth postoperative day, a bluish discolored area, slightly larger than a silver dollar, appeared on the dorsum of the right foot. The next day the area was definitely dry gangrene. On the seventh day, an identical, but slightly smaller area was evident on the left foot. A week later, the sloughs were easily lifted off, leaving clean ulcers and showing that the process had involved the entire thickness of the skin. The edema subsided rapidly following the appearance of the gangrenous areas. While gangrene was present, palpation of the terminal vessels was difficult. The popliteal and posterior tibials were felt, but there was some question about the



Fig. 2.—Left foot seven days post-



Fig. 3.—Same foot two days later, showing gangrene. Similar lesion on right foot.

dorsalis pedis. After the edema had disappeared these also were felt. The ulcers healed without difficulty.

On the seventh day the patient developed signs in the right lower lobe of the lung, which were diagnosed pneumonia, but in view of the gangrene and metastatic abscesses, it is entirely possible that this was an infarct. This cleared up, but left some fluid, which was still present at the time of discharge.

Sixteen days postoperative, the skin over the anterior, lateral, and posterior surfaces of the lower third of the right leg became discolored and swollen, and presented much the same appearance as the skin over the dorsum of the feet, before it became gangrenous. However, this developed into three localized abscesses, which were opened eight days later, and from which pure cultures of an anaerobic streptococcus were obtained.

On the forty-second day, the medial surface of the upper third of the right thigh became painful, swollen, and very hard. Eighteen days later, a deep abscess was opened and about 200 e.e. of pus obtained, cultures of which showed the same organism found in the abscesses of the leg. The temperature immediately dropped, and recovery was rapid. The patient was discharged on the eightieth day.

We believe the lung condition can be accounted for by an embolus from a pelvic thrombophlebitis and the abscesses, by bacterial thrombi. The gangrene was of the dry type and evidently due to complete obstruction of a very small artery, either by an embolus, which passed through the pulmonary circulation, or the development of an arteritis from bacteria with thrombosis and obliteration.

Brief abstracts of the 22 additional cases noted in the literature since 1925 follow:

Toll.—Aged twenty-six, gravida 9, spontaneous delivery. Up on fourth day. On fifth day chills and fever. Gangrene of both legs to just below knees. Amputation, recovery. Examination of legs showed arteries empty, veins filled with bloody viscous fluid. Condition attributed to arterial obstruction from endarteritic changes brought on by infection.

Entwisle.—Aged forty-four. Premature delivery at seven months. Chills, first two weeks postpartum. Gangrene of left leg to knee. Death.

King, Miller and Houser.—Aged thirty-seven, gravida 10. Normal delivery. No fever. Gangrene of both feet and legs, extended in spite of amputation, and patient died on table from pulmonary embolism when amputation at hip was being performed. Antopsy showed thrombosis of aorta from 1.5 cm. above the bifurcation, down.

Hicks.—Aged twenty, gravida 3. Normal delivery. Onset four weeks postpartum with edema. Two weeks later gangrene to knees. Amputation, recovery. Legs showed thrombosis of anterior and posterior tibial arteries and thrombi in all veins.

Portteus.—Aged twenty-five, gravida 1. Long labor, twins, hemorrhage, shock. Chills and septic temperature. Four weeks postpartum moist gangrene of both feet. Double amputation on fifty-second and fifty-sixth days. Death on eighty-seventh day from pneumonia.

Behne.—Aged thirty-seven, gravida 9. Spontaneous delivery. Twelve days postpartum gangrene of right leg developed, amputation. Death on thirty-fifth day. Autopsy showed thrombosis of right anterior and posterior tibial arteries, general peritonitis, mitral stenosis with thrombotic endocarditis doubtless causing the lesion in the leg.

Bartels and Estrin.—Aged thirty-seven, gravida 7. Premature delivery. Chills and fever during labor, amniotic fluid foul. Gangrene of left leg. Amputation at upper third of thigh on twentieth day. Discharged in good condition, seventy days later. Leg showed thrombi in arteries and veins. A facultative anaerobe and a short gram-positive bacilli, similar to Franke's gas bacillus, were found in the leg.

Pall.—Aged thirty-two, gravida 6. Entered hospital with infected incomplete abortion. Blood culture positive for hemolytic streptococci. Five days later whole right leg cool and cyanotic, and beginning to show gangrene. Died before line of demarcation formed. Autopsy findings: septic endometritis; thrombus 5 cm. long in femoral artery, containing many bacteria.

O. Schmidt.—Case 1.—Aged twenty-three. Curetted and packed outside of hospital. Entered hospital with appearance of sepsis. Six days later both hands and feet became livid and cool. Portions of toes sloughed off. Lost all toes but one on right foot and three from left. Hands recovered.

Case 2.—Aged thirty-eight. Curetted eight days after supposed abortion, but later found by culdesac puncture to have tubal pregnancy. Fever for four days. Patient was up on eleventh day. One week later she collapsed from lung emboli.

In a few days gangrene of right leg at knee. Amputation and death. The leg showed embolus in femoral artery.

The following cases are those in which gynergen or ergot were used.

O. Schmidt.—Case 3.—Aged twenty-six, gravida 2. Spontaneous delivery. Slight fever. On ninth day temperature 39° C. Hands and feet painful and blue. Hands recovered, but there was superficial gangrene of toes of one foot. Patient was given gynergen, 1 c.c. after delivery and one tablet per day for first six days.

Kienlin.—Aged thirty-four, gravida 2. Spontaneous delivery. On eleventh day, thrombosis of both femoral veins. On eighteenth day right foot discolored and no pulse felt in right tibial artery. Six days later, blisters on right leg. Spontaneous recovery. Condition explained on basis of gynergen and angioneurotic edema.

Neumann.—Aged twenty-three. Entered hospital with chills following criminal abortion. Had had rheumatism and endocarditis for twelve years. Septic endometritis and parametritis. Gangrene of left foot and leg to knee developed. Amputation and recovery. Leg showed no thrombi or emboli, only marked contraction of arteries. Received 5 mg. of gynergen by injection twice daily for six days and six tablets daily for nineteen days.

Simonovitis.—Spontaneous febrile abortion. On fifteenth day gangrene of two toes. Conservative treatment and recovery. Gynergen given three times daily for four days.

Moskowitz.—Aged thirty-five, gravida 2. Spontaneous delivery after thirty-six hours' labor. Puerperal fever. For six days "Sekalfluidextrakt" was given three times daily (0.375 gm.), followed by definite signs of ergot poisoning, collapse, weakness in limbs, itching, etc. No pulse in radial, popliteal, or arteries of feet. Superficial gangrene appeared on backs of feet and toes. Complete recovery in ten weeks. The lesion in this case is similar to ours in which no ergot was used.

Speizer.—Aged twenty-five, gravida 2. Marked varicosities and edema of legs. Postpartum hemorrhage. Septic fever on tenth day with double pelvic masses. On seventeenth day, no pulsation in right dorsalis pedis artery. On twenty-eighth day foot discolored. On thirty-third day died of peritonitis. At autopsy, there was gangrene and thrombosis of femoral and dorsalis pedis veins. Patient received 8 c.c. gynergen after delivery and three tablets daily for five days.

Lork.—Case 1.—Aged thirty-two, multipara. Normal labor. Febrile puerperium. Gangrene of both feet and amputation on thirty-eighth day. Recovery. Given one tablet gynergen three times daily, total dose equivalent to 36 mg. "ergotamin."

Case 2.—Aged thirty-four, gravida 2. Spontaneous delivery. Manual removal of placenta from bicornuate uterus. Febrile puerperium. Gangrene of right foot. Amputation and recovery. Gynergen three times daily for thirteen days (equal to 39 mg. "ergotamin").

Goldberger.—Aged twenty-six, gravida 4. Febrile abortion. Intraperitoneal streptococcus abscess drained through culdesac on seventh day. Parasthesia of both legs developed, followed by disappearance of popliteal and dorsalis pedis pulses. Periarterial sympathectomy done on left side, which became worse than the right. Slow recovery over period of months. The capillary microscope showed affections of the vascular nerves. Patient had been given 1 cm. gynergen daily and 12 drops three times daily by mouth.

Caffier.—Aged twenty-five. Several pieces of retained placenta removed. Fever. On twenty-second day feet cool and edematous. Two weeks later both feet bluish black except one great toe. One week later line of demarcation at edge of toes. Second and fifth toes of right foot dropped off. On left, all toes recovered but one. Ergot had been given for nineteen straight days.

Brandies.—Aged twenty-two. Entered hospital with chills and fever after injecting soap solution into uterus. Aborted spontaneously next day. Black dis-

coloration continued from feet up to middle of leg. Portions of skin fell off, exposing tendons. Treated conservatively and recovered. One e.e. of gynergen given after abortion and two tablets a day for three days.

Heyer.—Aged twenty-four, multipara. Abdominal pain and fever three weeks before entering hospital. Four days later early placenta removed from uterus with finger. Eight days later discoloration of feet and lower third of legs. Eight days later a line of demarcation two fingerbreadths above malleolas in left and three on right. Double amputation. Recovery. Only findings in arteries were marked contraction and narrowing of lumen. Occasional organizing thrombus in veins. Three tablets of gynergen were given daily for several days. Author feels that the small amount of gynergen could not be responsible because patient had a neurospastic diathesis, for frequently her hands and feet would fall asleep.

The two following cases are abstracted, because they occurred during the puerperium; but, they are not included in the totals, because it seems unlikely that the delivery or abortion was responsible for the lesions, and the authors definitely attribute them to other causes.

Stevens.—Aged thirty-one, gravida 3. Normal delivery. Pain and burning in right index finger three weeks before delivery. Gangrene six days postpartum. Amputation. Recovery. Patient had no signs of infection and author attributes ease to endarteritic changes.

Polano.—Aged thirty-six. Abortion done at three months for tuberculosis. Radial pulse not palpable on seventh day. On the fourteenth day gangrene of fingers of left hand. After two years a griffen claw contraction of two fingers occurred. A diagnosis of beginning Raynaud's disease was made by neurologists. Received one tablet of gynergen three times a day for five days.

SUMMARY

Puerperal gangrene is a rare and serious complication.

The lower extremities are most frequently involved.

It is due to obliteration of the circulation of the affected part, arterial or venous.

Infection is the common etiologic factor.

With the use of gynergen, an increasing number of cases are reported in the German literature.

It is questionable whether gynergen is the primary factor, because in all the cases but one there was infection.

REFERENCES

Bartels, A., and Estrin, A.: Zentralbl. f. Gynäk. 51: 502, 1927. Behne: Zentralbl. f. Gynäk. 41: 1297, 1921. Brandies, T.: Zentralbl. f. Gynäk. 52: 620, 1928. Caffier, P.: Ztschr. f. Gynäk. 92: 116, 1927. Entwisle, R. M.: Atlantic Med. J. 27: 360, 1924. Goldberger: Zentralbl. f. Gynäk. 25: 1928. Heyer: Zentralbl. f. Gynäk. 51: 1718, 1927. Hicks, C. F.: West Virginia Med. J. 13: 337, 1919. King, E. L., Miller, M. O., and House, G. H.: Ann. Surg. 87: 767, 1928. Kienlin, K.: Zentralbl. f. Gynäk. 52: 622, 1928. Lork: Monatschr. f. Geburtsh. u. Gynäk. 80: 17, 1928. Moore, S.: A. J. Roentgenol. 10: 507, 1923. Moskowitz: Abstracted by Sanger: Zentralbl. f. Gynäk. 53: 586, 1929. Neumann: Monatschr. f. Geburtsh. u. Gynäk. 80: 831, 1928. Pall, G.: Zentralbl. f. Gynäk. 51: 3246, 1927. Polano: Monatschr. f. Gynäk. 79: 164, 1927. Portteus, W. L.: Indianapolis Med. J. 33: 82, 1930. Saenger, H.: Zentralbl. f. Gynäk. 53: 586, 1929. Schmidt, O.: Zentralbl. f. Gynäk. 41: 1297, 1921. Simonovitis: Abstracted by Sanger: Zentralbl. f. Gynäk. 53: 586, 1929. Speizer: Zentralbl. f. Gynäk. 28: 1928. Stein, A: Surg. Gynec. Obst. 23: 424, 1916. Stein, A.: Surg. Gynec. Obst. 9: 595, 1925. Stevens, M. J.: Canada Med. Assn. J. 20: 642, 1929. Toll, R. M.: Am. J. Obst. & Gynec. 16: 108, 1928.

BLOOD GUANIDINE BASE CONCENTRATION IN ECLAMPSIA

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PARATHYROIDECTOMY in animals is accompanied by retention of guanidine in the blood, as shown by Paton and Findlay,1 Burns,2 and Bayer.3 An increase in blood guanidine concentration has also been found in active tetany in children² and in arterial hypertension.4,5 Watanabe6,7,8,9 reported studies on the influence of administration of guanidine bases upon the blood-sugar content and upon urinary ammonia and acid excretion. He found that the subcutaneous injection of a 10 per cent solution of guanidine hydrochloride into rabbits induces symptoms almost identical with those of tetania parathyreopriva, as well as a hypoglycemia. This author suggests that the hypoglycemia following parathyroidectomy may be due to the action of guanidine, which increases in the blood under these conditions. He further found, following the administration of guanidine, an excess of ammonia, and a decrease in acid elimination in the urine, resulting in severe acidosis with retention of phosphates and a decrease of calcium in the blood; and concludes that it is possible that the fundamental cause of tetany is the increased formation of guanidine nitrogen brought about by a disturbance in the function of the parathyroid.

Major and Weber⁴ reported slight increases in blood guanidine in patients with arterial hypertension, and quite marked guanidine retention in severe chronic nephritis and uremia. Major cautiously concludes that certain hypertensives show in their blood an increased amount of some substances giving the same color response as guanidine and having certain chemical properties similar to those exhibited by the guanidine bases.

Recently Ellsworth¹⁰ observed an increase in blood guanidine in patients with arsphenamine jaundice, in which diffuse liver damage is known to occur, as well as in patients with Laennee's cirrhosis of the liver. Minot and Cutler¹¹ had previously shown that dogs, fed on a meat diet low in calcium, are very susceptible to carbon tetrachloride poisoning, and that the administration of calcium, after intoxication had started, usually cured the condition. They further found that the liver necrosis produced by carbon tetrachloride or chloroform was accompanied by a hypoglycemia and by a retention of guanidine in the blood. In an investigation upon acute liver injury,¹² these authors concluded that in certain types of liver disease and also in eclampsia, the same abnormalities in blood chemistry, namely increased guanidine and hypoglycemia, are present as in their dogs with carbon tetrachloride and chloroform intoxication. They further stated that calcium medication gave prompt relief in their patients with preeclamptic toxemia, eclampsia, and liver disease.

Since the work of Major and Weber,4 on blood guanidine in hypertension, we have been interested in the guanidine bases in eclampsia and have routinely made guanidine determinations on the blood of our eclamptic patients during the past three years.

METHODS

We employed the method of Major and Weber.⁵ In a personal communication, Major states that he has good evidence to believe that the color reaction in this method is due to a guanidine compound, although it is difficult to say positively that it is methyl guanidine. Major and Weber suggested that a creatine correction should be made, and we have accordingly determined creatine and creatinine both on the original Folin-Wu filtrate, as well as on 2 e.c. of extract set aside for that purpose, as they suggest. In our determinations the final creatine figures on the extract were usually lower than those on the original filtrate, and because of that discrepancy we have not applied the correction to the guanidine values.

Blood-sugar determinations were made by the Benedict method of 1925, 13 Co₂-combining power by the van Slyke procedure, nonprotein nitrogen and uric acid by the methods of Folin, 14 . 15 and the chlorides by the method of Whitehorn.

In Table I are reported the nonprotein nitrogen, uric acid, sugar, CO_2 -combining power and guanidine values in the blood of normal pregnant women at term. The blood sugar in these patients ranged between 67 and 81 mg., with an average of 73 mg. per 100 e.e. It should be noted that by the method of Benedict, which we employed, the normal blood sugar is about 75 mg. per 100 e.e. of blood. The "guanidine" values ranged between 0.22 and 0.40 mg., the average being 0.33 mg. per 100 c.e. of blood. The other blood constituents reported are in agreement with ...gures given in earlier publications.¹⁷

TABLE I. NORMAL PREGNANT UMEN AT TERM

CASE NO.	NONPROTEIN NITROGEN	URIC ACID	SUGAR	CO_2	GUANIDINE
1	33.1	3.0	67	46.6	0.22
2	28.2	2.8	76	45.7	
3	27.0	2.8	69	44.7	0.38
4	28.5	2.0	71	46.6	
5	30.6	2.7	81	50.4	0.40
Average	29.5	2.7	73	46.8	0.33

The same blood constituents were also studied in 23 eclamptic patients during the past three years. The findings are recorded in Table II. All values are given in mg. per 100 c.c. blood, except the CO₂-combining power which is reported in volumes per cent. In this work we still used the original Folin-Wu filtrate and consequently the figures are for laked blood, although Folin¹⁶ recently suggested the use of unlaked blood.

From a comparison of the findings in eclampsia with those in normal pregnant women at term, we must conclude that our eclamptic patients did not show a definite or marked increase in blood guanidine, nor a hypoglycemia; and in this respect our results are at variance with those of Minot and Cutler. It should be noted that the

eclamptic patients show an increased uric acid content in the blood and a decreased CO₂-combining power.

TABLE II. ECLAMPTIC PATIENTS

CASE NO.	NONPROTEIN NITROGEN	URIC ACID	SUGAR	CO ₂	GUANIDINE
6	28.5	3.2	105	50.2	0.39
7	61.8	8.6	82	29.1	
8	33.3	6.1	73	35.6	
9	34.5	9.4	87	50.5	
10	32.5	11.4	80	38.8	
11	35.3	4.7	75	31.8	0.29
12	41.9	5.6	89	35.7	
13	29.7	4.0	59	49.2	0.40
14	46.0	9.2	50	38.5	
15	34.9	6.1	58	45.5	
16	46.0	4.8	98	40.0	
17	35.0	7.0	167	24.0	
18	39.5	6.0	167	22.1	
19	40.0	3.9	91	51.3	
20	37.5	4.4	61	48.5	0.26
21	31.6	6.1	105	30.3	0.38
22	30.0	3.8	47	47.5	0.39
23	32.1	4.5	55	44.7	0.28
24	38.7	5.6	66	38.1	0.49
25	54.6	3.6	93	39.0	0.58
26	26.1	4.0	69	39.5	0.48
27	29.3	6.7	109	33.4	0.32
28	40.0	7.0	130	41.9	
Average	37.33	5 0	87.7	39.3	0.39

TABLE III. BLOOD CHEMISTRY OF NORMAL RABBITS

RABBIT NO.	NONPROTEIN NITROGEN	UREA NITROGEN	URIC ACID	CHLORIDES	SUGAR	CO_2
7	43.6	19.6	0.7	447	75	37.5
12	46.8			419	109	40.8
13	50.0		0.8	446	95	48.5
16	35.7	12.3	0.7	432	108	54.2
Average	44.0	16.0	0.7	436	97	45.2

At the conclusion of the experiment the animals were sacrificed in order that the various tissues might be studied histologically. The chemical and histologic findings are summarized in Table IV, which should be compared with Table III, giving the findings on four normal rabbits.

TABLE IV. RABBITS-GUANIDINE ADMINISTERED

NO.	WEIGHT	DATE	GUANIDINE INJECTED	TIME OF VENI-	NON- PROTEIN NITRO- GEN	UREA NITRO- GEN	URIC	CHLO- RIDES	SUGAR	00	GUANI- DINE	CONDITION AND PATHOLOGY
1	2050	3/8/26	8/29 0.25 gm. hydrochloride	9:30 A.M.	43.6	19.6	0.7	447	75	37.1	0.2	Comatose after injection. Killed
			per kilogram at 10 11:00 A.M.	11:00 A.M.	44.1	20.1	8.0	405	80	30.0		at 11:30 A.M. Liver normal.
00	2300	3/22/29 0.26	9 0.26 gm. hydrochloride	11:10 A.M.	44.6		0.7		86	34.0		Muscular twitchings after injec-
			A.M. A.M.	12:35 P.M.	84.8	20.1	1.1	459	118	11.4	7.50	tion. Coma. Death at 1:15 P.M. Liver normal.
6	3405	3/26/28	3/26/29 0.05 gm. methyi guani- dine sulphate per kilo-3/26/29 gram at 10 a.M. In-	9:30 A.M. 3/26/29	39.1				100	42.1		No symptoms over 10 days of experiment. Killed 4/6/29.
			jection repeated, same 11:40 A.M. dosage, on 5 successive 4/6/29 days.	11:40 A.M. 4/ 6/29	38.7	15.4	8.0	495	80	39.4	deli come antone granda della come della com	infiltration. No necrosis. Kidneys normal.
10	1500	3/26/28	ydrochloride am at 10 ion repeat	9:00 A.M. 3/26/29 Clotted								No symptoms or signs. Killed at 11:10 A.M., 4/10/29. Liver normal. Kidneys normal.
			same dosage, on five successive days.	five 11:00 A.M. 126.0 4/10/29	126.0	66.7	6.0	619	98	26.6		
14	2500	4/ 5/29 0.35 din	0.35 gm. methyl guani: 10:40 a.M. dine per kilogram at 11:05 a.M.	10:40 A.M.	58.8		1.6	447	121	38.5		Had several convulsions immediately after injection. Killed at 11:15 A.M., 4/5/29. Liver
				11:10 а.м. 138.0	138.0		1.7	389	140	40.1		- co
9	2000	3/20/29 0.25 ki	0.25 gm. sulphate per 9:30 A.M. kilogram at 10:00 Clotted A.M.	9:30 A.M. Clotted								Convulsions immediately after injection. Coma. Killed at 11:59 A.M., 3/20/29. Liver
				11:55 A.M.	85.6		2.4	439	500	9.1		showed fatty infiltration with moderate central necrosis.

DISCUSSION OF FINDINGS

The results recorded in Table IV show a lowering, sometimes very marked, in the CO₂-combining power following the intravenous injection of guanidine in rabbits. Shortly after the injection, the blood sugar may show a hyperglycemia, as was also demonstrated by Watanabe, and later a hypoglycemia. In our experiments we did not follow the blood sugar at frequent intervals over a long period of time, as the findings of Watanabe in this respect are quite conclusive. He found that in all his rabbits hypoglycemia developed several hours after the administration of guanidine. The other blood constituents studied by us revealed nothing abnormal except that in several of the animals the nonprotein nitrogen and urea nitrogen were elevated, while the blood chlorides decreased in two and increased in one animal following the injection.

The histologic study of the liver showed that the administration of guanidine produced no lesion comparable with the accepted eclamptic peripheral necrosis. Indeed, in most of our animals the liver was normal, or at most revealed a generalized fatty infiltration.

Returning to the findings in the blood constituents in eclampsia as recorded in Table II, we note that the disease is accompanied by a normal or slightly elevated nonprotein nitrogen, an increase in uric acid, a normal or increased blood sugar, a decrease in the CO2combining power and a normal "guanidine" content. It should be remembered that in the blood-sugar determinations we employed the 1925 Benedict method, which gives a normal of about 75 mg. per 100 c.c. blood. Our average is 73 mg. for normal pregnant women at term, as compared with 87.7 mg. in eclamptic patients, while in only 9 of the latter did the blood sugar fall below 75 mg. The lowest bloodsugar value in our eclamptic patients was noted in Case 22, where it was 47 mg. It must be pointed out, however, that we occasionally have encountered equally low values in normal pregnancy. On the basis of our findings, we cannot agree with Minot and Cutler that there is a tendency to hypoglycemia and a definite elevated blood guanidine in eclampsia, as in our cases normal blood sugar or an actual hyperglycemia is seen far more frequently than hypoglycemia.

Minot and Cutler,¹² finding hypoglycemia and elevated blood guanidine values in eclampsia report the successful use of intravenous administration of calcium (Sandoz Company's sterile ampules) in a few patients suffering from this disease. Contrary to the reports of these authors, Watanabe⁷ found that in animals with guanidine hypoglycemia injection of ealcium lactate failed to restore the blood-sugar content to normal.

As long ago as 1923 we tried calcium therapy in the treatment of eclampsia on the basis of a suspected decrease in this cation in the blood of patients suffering from the disease. In this connection the following protocol may be of interest:

Patient M. B-11, J. H. H. history No. 12,513, a sixteen-year-old colored primipara at term was admitted May 31, 1923, after having one convulsion. Diagnosis: antepartum eclampsia; confirmed later by autopsy.

5/31/23	B. P. 150/100	2nd convulsion.
6/1/23	B. P. 170/120	3rd convulsion. Labor started at 7:00 P.M.
6/ 2/23	B. P. 170/110	4th convalsion. In labor.
6/ 3/23	B. P. 170/110	5th to 13th convulsion. Delivered, low forceps.
6/ 4/23	B. P. 160/100	13th to 21st convulsion. Unconscious since delivery.
6/ 5/23	B. P. 140/60	21st to 37th convulsion. Death at 6:10 P.M.

The following note, written by the author, is taken from the history: "6/5/23: Analyses on patient's serum showed the following:

Na	370.0	mg.	per	100	e.e.	serum	
\mathbf{K}	31.0	mg.	per	100	e.e.	serum	
Ca	9.1	mg.	per	100	c.c.	serum	
Mg	2.5	mg.	per	100	e.e.	serum	

From these figures it is evident that the ratio $\frac{[Na] + [K]}{[Ca] + [Mg]}$ is increased over normal. With this in view it was thought advisable to give the patient calcium chloride with an idea of reducing this ratio. Since she was in coma, it was necessary to administer the $CaCl_2$ intravenously. Four injections, two on the fourth and two on the fifth of June were given. The total Ca given was 1.21 gm. This raised the Ca in the serum to 10.1 mg. per 100 e.c.' We had a similar experience in another case in 1924.

Subsequent work¹⁷ on the cation ratios in eclampsia has convinced us that calcium therapy is not necessary to attempt to restore these ratios to normal, as the disease is accompanied by no abnormal shift in any of the ratios, except a slight increase in $\frac{[P]}{[Ca]}$ due mainly to a slight increase in phosphorus. Furthermore, calcium therapy does not seem indicated in this disease on the basis of blood sugar or blood guanidine content, as hypoglycemia and increased blood guanidine content are not the usual findings in eclampsia.

CONCLUSIONS

- 1. Blood "guanidine" is not markedly elevated in eclampsia.
- 2. Hypoglycemia is not a usual accompaniment of eclampsia.
- 3. Intravenous administration of guanidine in the rabbit in doses ranging from 0.05 to 0.25 gm. per kilogram of body weight, does not produce liver necrosis.
- 4. Calcium therapy in eclampsia does not appear rational on the basis of blood guanidine, blood sugar, or blood cation ratios.

REFERENCES

(1) Paton, D. N., and Findlay, I.: Quart. J. Exper. Physiol. 10: 315, 1916. (2) Burns, D., and Sharp, I. S.: Quart. J. Exper. Physiol. 10: 345, 1916. (3) Bayer, G.: Ztschr. f. d. Ges. Exper. Med. 27: 119, 1922. (4) Major, R. H., and Weber, C. J.: Bull. Johns Hopkins Hosp. 40: 85, 1927. (5) Major, R. H., and Weber, C. J.: Arch. Int. Med. 40: 891, 1927. (6) Watanabe, C. K.: J. Biol. Chem. 33: 253, 1918. (7) Ibid. 34: 51, 1918. (8) Ibid. 36: 73, 1918. (9) Ibid. 36: 531, 1918. (10) Ellsworth, R.: Bull. Johns Hopkins Hosp. 46: 296, 1930. (11) Minot, A. S., and Cutler, J. R.: J. Clin. Invest. 6: 369, 1928. (12) Minot, A. S., and Cutler, J. R.: Proc. Soc. Exper. Biol. & Med. 26: 607, 1929. (13) Benedict, S. R.: J. Biol. Chem. 64: 211, 1925. (14) Folin, O., and Wu, H.: J. Biol. Chem. 38: 81, 1919. (15) Folin, O.: J. Biol. Chem. 54: 153, 1922. (16) Folin, O., and Svedberg, A.: J. Biol. Chem. 83: 85, 1930. (17) Stander, H. J., Duncan, E. E., and Sisson, W. E.: Bull. Johns Hopkins Hosp. 36: 411, 1925.

A PROPOSED MODIFICATION OF THE ASCHHEIM-ZONDEK "PREGNANCY TEST"*

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BEFORE presenting our modification of the Ascheim-Zondek reaction, in view of the large amount of experimental work that has been done concerning the function of the anterior pituitary lobe, it seems advisable to abstract the literature in order to obtain a chronologic review of the results.

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Thus far no reference has been found in the literature on the use of blood serum intravenously in rabbits, followed by observation of the ovaries at operation or autopsy for any reaction from the anterior pituitary hormone. Apparently absorption of the hormone from the anterior lobe of the pituitary is directly through its vascular supply. It seems logical to expect a rather constant hormone level in the blood stream since any excess may be liberated through the kidney.

In our laboratory a series of 23 rabbits weighing from 600 to 1,700 gm. was injected with 5 c.c. of urine from various cases. Autopsies were performed between seventeen and one-half and forty-nine hours after injection and the earliest time at which definite hemorrhagic follicle formation was observed was thirty and one-fourth hours. Of 13 known cases of pregnancy, 5 gave positive reactions grossly; 6 cases were examined at or before twenty-four hours after injection and did not give a positive reaction grossly, but all were positive on microscopic examination; 2 rabbits injected with urine from a case at term showed doubtful reactions grossly after forty hours, but were positive micro-

*Presented as a preliminary report at the St. Louis Medical Society, December 16, 1930.

Note: For lack of space it is not possible to print Dr. Brown's article in full. The complete paper is published in the author's reprints. The elided paragraphs are marked by * * * * *.—Editor.

scopically. Nine cases not pregnant gave no reaction. One rabbit died forty-five minutes after injection. The doubtful reactions were largely due to the examination of the ovaries at too early a time, because in some of the duplicate animals allowed to go for a longer time, the reaction was definitely positive. It is probably best to examine the ovaries between thirty-six and forty-eight hours after injection by this method. The results would have been more constant if older rabbits had been used. 35

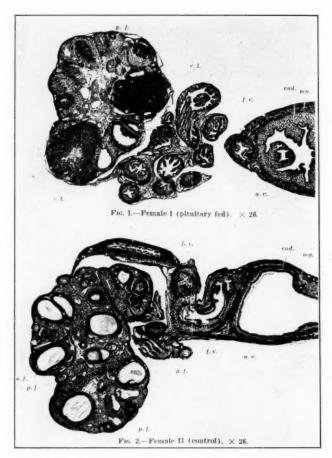


Fig. 1.—Reproduction from article by Emil Goetsch in Bulletin of Johns Hopkins Hospital, 1916, showing effect upon the ovary of feeding pituitary extract (whole gland) for forty-two days as compared with a control rat.

As the results of the intravenous injection of urine were only partially satisfactory, blood serum was used next. Five e.e. of serum from a case of known pregnancy of four months' gestation were given intravenously and the rabbit autopsied in thirty-one hours. The ovaries were found to be enlarged and to contain numerous hemorrhagic follicles. The uterus also showed the results of great activity by marked swelling

and injection, probably due to the presence of the ovarian hormones in the serum.

Following this a series of 35 rabbits was injected intravenously with from 2 to 5 c.c. of serum and the earliest definitely positive reaction obtained was at thirteen hours. Numerous doubtful reactions were obtained with serum from known pregnancies when the rabbits died too soon or were autopsied too early. Of the series 7 rabbits died at various intervals, but only one was too early to show any reaction. One rabbit dying one and one-half hours after injection, showed marked congestion of the uterus and enlargement of both ovaries with developing hemorrhagic follicles seen microscopically. Of 24 rabbits injected with serum from known cases of pregnancy, 18 gave definitely positive results grossly. Another of these cases when autopsied at twenty-five hours, was doubtful grossly, but positive microscopically. Five other cases were doubtful or negative grossly when the rabbits died before thirteen hours had elapsed, but these were all positive microscopically. A doubtful reaction in the gross was obtained when serum was injected from a case which was one week postabortion, but microscopically this was positive. Five cases which were not pregnant gave negative results. A case of hydatidiform mole gave a very well marked positive reaction. The specimens giving positive reactions in the gross were obtained at from three weeks' to seven months' gestation. A positive test was obtained by the use of plasma instead of serum in one case of four months' gestation. Spinal fluid from a case of eight months' gestation gave a negative reaction. A case of questionable pregnancy of ten to twelve weeks with splenomegaly gave 3 negative reactions.

TABLE I

Positive reaction grossly with known pregnancy	18
Doubtful reaction grossly with known pregnancy at 25 hours,	,
but positive microscopically Death too soon (within thirteen hours) after injection to give	1
definite reaction grossly, but positive microscopically	5
Death occurred at 30 minutes, no reaction grossly or micro- scopically	1
Negative reactions with known pregnancy	0
Negative reaction in a case of splenomegaly with question of	
pregnancy	3
Doubtful reaction grossly 7 days after abortion, microscop-	
ically positive	1
Case of hydatidiform mole	1
Negative reactions with no pregnancy	5
	-
Total number of rabbits injected with serum	35

Of the 24 positive cases, 18 (75 per cent) gave a positive reaction grossly, and 6 (25 per cent) doubtful gross reactions were positive microscopically. There were no negative reactions with sera from cases of known pregnancy. The percentage of grossly positive reactions in-

ereased considerably toward the end of the series as the technic was improved.

Several of the rabbits in this series were operated upon in order to examine the ovaries after injection of serum, and these were used again three weeks later, giving definitely positive results. The rabbits which died following the injection of serum intravenously were in the early part of the series when an attempt was being made to parallel the tests



A B

Fig. 2

Fig. 3

Fig. 2.—Contrast of effects produced by equal amounts of (A) urine, and (B) serum (the latter about two times as marked) intravenously in rabbits. Fig. 3.—Results from injection of (A) 2.4 c.c. and (B) 4.0 c.c. serum respectively (reaction in proportion to dose).

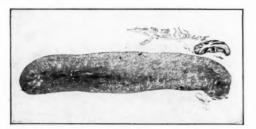


Fig. 4.—Low-power magnification of normal rabbit ovary.



Fig. 5.—Lower-power magnification (same as in Fig. 4) of reacting rabbit ovary.

with those in which urine was given intravenously. The animals showed evidence of toxic reaction to the serum. The dose of 5 c.c. was too often fatal and was soon reduced. From this series the conclusion was drawn that approximately 1.0 c.c. of serum could be given for every 700 gm. body weight without being toxic and still produce the reaction.

When equal amounts of urine and serum were given to rabbits of the same weight and the tests allowed to run for the same interval of time, the contrast was very marked, the reaction from the serum apparently about twice that from the urine (Fig. 2). A similar contrast was noted between the reactions to various amounts of serum, proportional to the dose (see Fig. 3). With a larger dose the "crop" of hemorrhagic follicles is increased. A considerable number of the follicles observed in this series showed the site of rupture even grossly. The time interval



Fig. 6.—Low power of hemorrhagic follicle ("Blutpunkt").

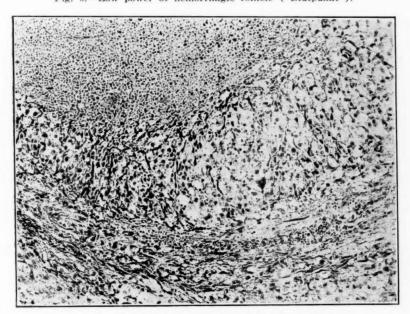


Fig. 7.—High power of area of beginning luteinization.

also seemed to play a part in the degree of reaction, which was noted in parallel tests when one autopsy was performed at twenty-four hours and the other at forty-eight hours.

Fig. 4 shows a low-power magnification of a normal rabbit ovary. Fig. 5 shows a similar magnification of a reacting ovary with the hemorrhagic follicles easily recognized. Fig. 6 shows a low power of a hemorrhagic follicle with luteinization commencing and this reaction is seen more clearly in the high power of this area in Fig. 7.

Whether the use of serum intravenously is of any more practical value as a "pregnancy test" than the other tests already devised, is not certain as yet. The important point to consider is that, by the intravenous injection of the serum of patients who are known to be pregnant, changes are produced in the ovaries and uterus of a rabbit which are entirely similar to the reaction observed in the Aschheim-Zondek "pregnancy test" but to a more marked degree.

SUMMARY

In the present modification of the Aschheim-Zondek test, 2 e.e. to 5 e.e. of serum were injected intravenously into the ear vein of a virgin female rabbit. Approximately 10 c.e. of whole blood are obtained from the patient and the serum is removed. The serum is allowed to stand for at least four hours or overnight before injection, as very fresh serum was found to be toxic and might cause death shortly after injection. The average effective amount of serum was found to be 1 c.c. per 600 to 700 gm. of body weight.

Rabbits weighing from 600 to 2,150 gm, were used. Animals weighing between 1,500 and 2,000 gm, gave the most constant results. A series of tests on the smaller rabbits proved to be very unreliable.

The rabbits were operated upon or autopsied from twenty-four to thirty-six hours after injection and the reaction could usually be determined by gross examination. Microscopic examination was used to check the gross findings. The rabbit could be used again at the end of three weeks.

The earliest grossly positive reaction was observed at thirteen hours. Several of the animals of this preliminary series died before thirteen hours had elapsed. The period of gestation varied from three weeks to seven months. Sera from 5 cases not pregnant were used and gave negative results. On a doubtful case of pregnancy, 3 tests were performed and were all negative. A case of hydatidiform mole gave a strongly positive reaction and was found to be negative three weeks later.

The reactions of the 25 positive specimens examined in this preliminary series were: 18 grossly positive; 5 doubtful grossly, but positive microscopically (rabbits died in less than thirteen hours); one autopsied at twenty-five hours was doubtful grossly but positive microscopically; one died thirty minutes after injection and showed no reaction.

The reaction to the use of serum intravenously is found to be definitely more marked and to appear in a shorter time than when urine is used intravenously.

CONCLUSION

The blood serum of pregnant women when injected intravenously into female rabbits results in the development of hemorrhagic follicles and luteinization in the ovaries due to the presence of the anterior pituitary hormone.

This reaction may be observed more definitely in the gross than is the case in the original Aschheim-Zondek "pregnancy test" and in one-fourth to one-third of the usual time.

(As this preliminary report goes to press, we wish to report that 220 tests have been performed by this method and the results have proved correct in almost 100 per cent of the cases.)

REFERENCES

(1) Compte, L.: Contribution à l'étude de l'hypophyse humain et de ses relations avec le corps thyroide. Lausanne, 1898; also Beitr. z. Path. Anat. u. z. allg. Path. 23: 90-110, 1898. (2) Erdheim, J., and Stumme, E.: Beitr. z. Path. Anat. u. z. allg. Path. 46: 1, 1909. (3) Schäfer, E. A.: Proc. Roy. Soc. 81: 453, 1909. (4) Crowe, S. J., Cushing, H., and Homans, J.: Bull. Johns Hopkins Hosp. 21: 160, 1910. (5) Aschner, B.: Arch. f. d. ges. Physiol. 146: 1, 1912. (6) Goetsch, E.: Bull. Johns Hopkins Hosp. 27: 29, 1916. (7) Goetsch, E.: Surg. Gynec. Obst. 25: 229, 1917. (8) Smith, E.: Science 49: 280, 1916. (9) Allen, B. M.: Science, xliv: 755-757, 1916. (10) Evans, H. M., and Long, J. A.: Anat. Rec. 21: 62, 1921. (11) Long, J. A., and Evans, H. M.: Anat. Rec. 18: 246, 1920. (12) Long, J. A. and Evans, H. M.: Anat. Rec. 1920. (12) Long, J. A., and Evans, H. M.: Memoirs of the U. of Calif. 6: U. of Calif. Press, 1922. (13) Long, J. A., and Evans, H. M.: Anat. Rec. 21: 57, 1921. (14) Long, J. A., and Evans, H. M.: Anat. Rec. 21: 60, 1921. (15) Zondek, B.: Arch. f. Gynäk. 120: 251, 1923. (16) Smith, P. E., and Engle, E. T.: Anat. 40: 159, 1927. (17) Zondek, B.: Deutsche med. Wehnschr. 53: 45, 1927. (18) Zondek, B., and Aschheim, S.: Klin. Wehnschr. 6: 248, 1927. (19) Aschheim, S.: Deutsche med. Wehnschr. 53: 45, 1927. (20) Zondek, B., and Aschheim, S.: Klin. Wehnsehr. 6: 249, 1927. (21) Aschheim, S.: Deutsche med. Wehnsehr. 53: 1246, 1927. (22) Aschheim, S.: Deutsche med. Wchnschr. 53: 1927, 1927. (23) Aschheim, S., and Zondek, B.: Klin. Wehnschr. 7: 1404, 1928. (24) Aschheim, S.: Klin. Wehnsehr. 7: 1453, 1928. (25) Engle, E. T.: Anat. Rec. 42: 16, 1929. (26) Evans, H. M., and Simpson, M. E.: Am. J. Physiol. 89: 371, 1929. Evans, H. M., and Simpson, M. E.: Am. J. Physiol. 89: 375, 1929. (28) Evans, H. M., and Simpson, M. E.: Am. J. Physiol. 89: 379, 1929. (28) Evans, H. M., and Simpson, M. E.: Am. J. Physiol. 89: 379, 1929. (29) Evans, H. M., and Simpson, M. E.: Am. J. Physiol. 89: 381, 1929. (30) Marshall: The Physiology of Reproduction. Longmans, Green & Co., 561, 1922. (31) Friedman, M. H.: Am. J. Physiol. 89: 438, 1929. (32) Friedman, M. H.: Am. J. Physiol. 90: 617, 1929. (33) Kelly, G. L., and Florence, L.: Surg. Gynec. Obst. 50: 435, 1930. (24) Flybrage, G. F., Avil. J. Open & G. F., Sylvage, 20: 1020. (25) Schmidter B. (34) Fluhmann, C. F.: AM. J. OBST. & GYNEC. 20: 1, 1930. (35) Schneider, P. F.: Surg. Gynec. Obst. 52: 56, 1931. (36) Schneider, P. F.: Proc. Soc. Exper. Biol. & Med. 28: 117, 1930. (37) Zondek, B.: Endokrinol. 5: 425, 1929. (38) Collip, J. B.: Canad. M. A. J. 22: 761, 1930. (39) Shirai, S.: Jap. J. Obst. & Gynec. 8: 220, 1930.

CHRONIC NEPHRITIS FOLLOWING APPARENT TOXEMIA OF PREGNANCY*

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A FOLLOW-UP study of the total cases of toxemia of pregnancy observed in the Obstetrical Department of the Johns Hopkins Hospital during the four-year period ending May 31, 1930, has recently been concluded by the author and M. L. Stout. It was the purpose of the study to reexamine as many as possible of these patients in an effort to ascertain how many of them eventually presented evidence of chronic renal involvement. Excluding toxemic vomiting and eclampsia, the return of two-thirds or 343 of the remaining patients was secured and definite signs of chronic nephritis were found in 137 (40 per cent) of them. In 1929, the author pointed out that 22 per cent of women suffering an attack of eclampsia will be found a year or more after delivery to have a definite nephritic process.

The correct diagnosis of nephritis had been made in the majority of these 137 women at the time of discharge from the hospital. A considerable number of them, however, had presented a rather mild process which apparently cleared up entirely during the early puerperium, so that the patients left the hospital with a normal blood pressure and with the urine free of albumin, and were considered at that time cases of low reserve kidney or preeclampsia. Likewise, a few of these patients were known to have had chronic renal disease prior to the onset of the pregnancy. Most of them already had hypertension, albuminuria, or symptoms indicative of toxemia when they first came under our observation for prenatal care. However, 29 of our nephritic women had registered in the Out-Patient department early in pregnancy and at that time had no hypertension, albuminuria, or symptoms. At the seventh month or thereafter, what appeared to be the clinical picture of low reserve kidney developed, or in a few instances, preeclampsia. In the majority of these patients the signs cleared up promptly in the early puerperium, yet at six weeks postpartum and thereafter, definite evidence of chronic nephritis was present. A brief analysis of these 29 cases together with 3 others which have been observed since, is the purpose of this paper, in which it is desired to stress the point that chronic renal damage has resulted from what clinically seemed to be a typical toxemia of pregnancy developing during or after the seventh month and in most cases apparently clearing up entirely in the early puerperium.

^{*}Read by invitation at a meeting of the New York Obstetrical Society, May 19, 1931.

Table I presents data on the 32 patients in the series according to race, age, parity, and previous history. It will be noted that approximately two-thirds of the women were black, and a similar proportion multiparae. The average age was 28.84 years, a figure five years above that of the general clinic material. In 9 instances there was a previous history of toxemia of pregnancy, while one patient had had rheumatic fever and another repeated attacks of tonsillitis. In two-thirds of the cases no history of previous disease predisposing to renal damage could be obtained.

TABLE I. STATISTICAL DATA ON PATIENTS IN SERIES 32

Race: White	10	Age: Average 28.84	years
Black	22	4 below age 20 8 above age 35	
Parity:		Previous History:	
Para 0	9	Toxemia	6
Para 1 and above	23	Eelampsia	3
Para 5 and above	10	Rheumatic Fever	1
Para 10 and above	5	Tonsillitis (repeated)	1

From a clinical point of view these patients prior to delivery presented the picture of a low reserve kidney or of a mild preeclampsia. Hypertension or albuminuria first appeared during the seventh month in 11 patients, and during the eighth month in 6, while in 15, or almost half of the total eases, the patient was apparently quite normal until at or near term. Table II indicates that the average high point

TABLE II. BLOOD PRESSURE AND ALBUMIN OBSERVATIONS

	PRIOR T DELIVER	_	DISCHARGE FROM HOSPITAL		6 WEEKS POSTPARTUM	4 OR MORE MONTHS POSTPARTUM
Blood Pressure			132.32		157.00	165.19
	116.88		89.1	9	104.25	105.13
Albuminuria	None	6	None	22	13	19
	Trace	8	Trace	8	2	3
	-1.9 gm, 2.0 gm,-	13 5	+	1	3	9

of blood pressure attained at the time of delivery was 170.5/116.88. In 5 instances the systolic pressure never reached 150 mm., while in only 4 was the high level of 200 mm. attained. Marked albuminuria (2 gm. or more per liter) occurred in only 5 patients, while in 7 casts were observed in the urine. It may be stated that the phenolsulphonephthalein and Mosenthal renal concentration test was done in 12 instances, but gave no information indicative of kidney damage. Thirteen patients had no edema at any time and only 3 presented marked water retention. In the majority of cases the eyegrounds were repeatedly examined but nothing to indicate nephritis was found.

The pregnancy was allowed to progress to term in 28 patients, and in 7 of them labor was induced at that time. In 1 patient there was a spontaneous premature termination of the pregnancy, while labor was induced several weeks before term in 3 others because of the toxemic process. Cesarean section was practiced in 5 instances, but in 4 of them the indication was that of pelvic dystocia. Thirty-three infants were delivered with 5 stillborn or neonatal deaths, three of which were due to prematurity.

During the early puerperium the blood pressure in some instances fell rapidly to normal, while in others the hypertension persisted.

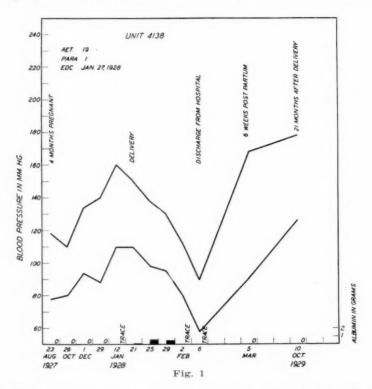
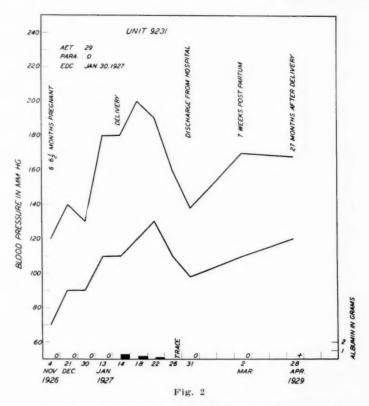


Table II indicates that the average pressure at the time of discharge from the hospital two weeks postpartum was 132.32/89.19, a reading near the upper limit of normal. If we accept a figure above 140/90 as indicating hypertension, 20 of these patients left the hospital with a normal pressure while in 11 instances the hypertension persisted. More than a trace of albumin was present in the urine of only one patient at discharge.

Eighteen of the 32 women returned to the dispensary for examination six weeks postpartum, while the remainder did not return until later. In 16 the blood pressure was taken and averaged 157.00/104.25, a figure indicating a mean rise of 25 and 15 mm. in the systolic and

diastolic readings, respectively, over that at the time of discharge. In 5 of the 18 cases albumin was present in the urine.

The patients in this series have all been under observation for at least four months and some of them for as long as four years since delivery. The average blood pressure at the present time, calculated on the basis of the latest dispensary reading, is 165.19/105.13, and 12 of them have some albuminuria. One patient died elsewhere two months postpartum, the clinical diagnosis being acute nephritis. Two patients have an essentially normal blood pressure but a marked and persistent albuminuria and have been diagnosed by the medical department as



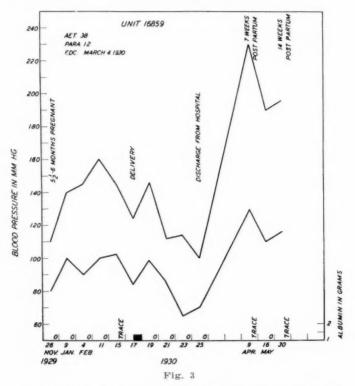
having nephrosis. Persistent hypertension and albuminuria are present in 10 cases, while in the remaining 19 the diagnosis was made on marked hypertension alone, a subsequent pregnancy complicated by nephritic toxemia being a substantiating factor in 5 of these.

A brief résumé of 5 rather typical cases from the series follows:

Case 1.—Unit 4138. (Fig. 1.) A nineteen-year-old black woman whose only previous pregnancy had been complicated by a mild toxemia which cleared up entirely in the puerperium. She again came under observation at the end of the fourth month of the second pregnancy, and at this time was quite normal, blood pressure 118/78, urine negative for albumin. The pressure rose gradually and two

weeks before term reached 160/110, albumin trace, slight edema of the ankles. Because of a contracted pelvis she was delivered by cesarean section. During the early puerperium the pressure fell, and she was discharged from the hospital on the seventeenth day after delivery with a pressure of 90/58, albumin trace. Six weeks postpartum the pressure had risen to 168/90 and twenty-one months after delivery the reading was 178/126, urine negative for albumin, severe headaches, afternoon edema, and beginning arteriosclerotic changes in the eyegrounds.

Case 2.—Unit 9231. (Fig. 2.) A twenty-nine-year-old black woman, who first was observed during the sixth month of her first pregnancy, blood pressure 120/70, urine negative. There was a rapid rise of pressure late in the pregnancy, reaching 180/110 just before delivery, with albumin appearing in the urine to the extent of

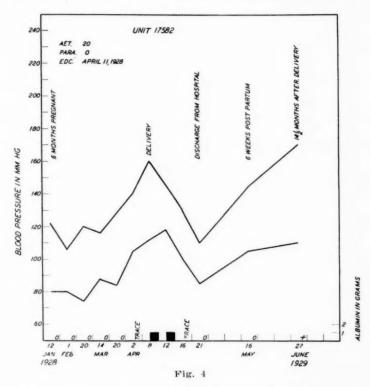


0.4 gm. per liter and marked edema. Following a spontaneous delivery the pressure fell somewhat, but not to normal, and she was discharged on the eighteenth day of the puerperium, blood pressure 138/98, urine free of albumin. Six weeks postpartum, there was an increased hypertension and twenty-seven months after delivery the pressure was 168/120, with albumin constantly present in the urine.

Case 3.—Unit 16,859. (Fig. 3.) A thirty-eight-year-old black multipara who first came under observation during the fifth month of her thirteenth pregnancy. Her obstetric career had hitherto apparently been uncomplicated. She developed a seemingly mild toxemia with the blood pressure reaching 160/102, a trace of albumin appearing in the urine, and slight edema. After a spontaneous delivery the pressure fell rapidly and she was discharged from the hospital on the eleventh day of the puerperium, blood pressure 100/70, urine negative. Six weeks postpartum the urine contained a trace of albumin and a marked hypertension was present, 230/130.

These findings persisted and she now has a pressure which is constantly around 200/120, albuminuria, headaches, and nycturia.

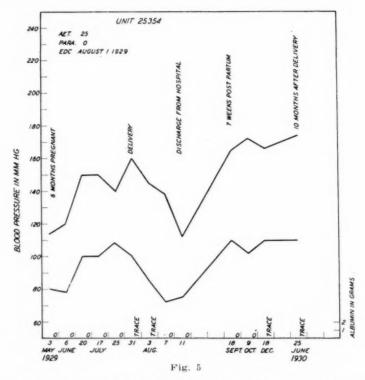
Case 4.—Unit 17,582. (Fig. 4.) A twenty-year-old black woman who was first seen during the sixth month of her first pregnancy, blood pressure 122/80, urine negative. An attack of rheumatic fever was the only item of interest in the past history. Near term, hypertension and albuminuria developed and for this reason labor was induced and terminated by low forceps. The pressure fell rapidly during the puerperium and at discharge on the fourteenth day postpartum was 110/85, urine negative. Six weeks after delivery a hypertension of 145/105 had developed and the condition progressed so that fourteen and one-half months after the pregnancy albuminuria was present, and the blood pressure had reached 170/110.



Case 5.—Unit 25,354. (Fig. 5.) A twenty-five-year-old black woman who came under observation at the sixth month of her first pregnancy, apparently normal in every way. Again a mild toxemic process developed and labor was induced at term. She was discharged from the hospital on the twelfth day of the puerperium with a pressure of 112/75, urine negative. Hypertension and albuminuria developed thereafter and ten months after delivery the pressure was 174/110, albumin trace, slight edema, headaches and nycturia.

DISCUSSION

We have previously shown that 22 per cent of eclamptic women will be found to have signs of chronic nephritis several months after delivery. Excluding this condition as well as vomiting of pregnancy, it has been found that 40 per cent of the remaining toxemic patients likewise show signs of renal involvement during the puerperium or later. Many of these undoubtedly had a frank nephritis prior to the pregnancy. However, a certain number of them clinically seemed to be suffering from a preeclampsia or low reserve kidney and were so treated on discharge from the hospital, yet they returned later with apparently definite nephritis. In this paper we have collected a series of 32 patients who came under observation at varying stages of pregnancy prior to the seventh month and at that time were without



symptoms, had a normal blood pressure and urine albumin-free. They developed signs of a clinically typical low reserve kidney or preeclampsia during or after the seventh month, which in most cases disappeared in the early puerperium. Six weeks postpartum or thereafter, these patients returned with evidences of chronic renal involvement which have persisted throughout their period of observation, varying from four months to four years.

We cannot say with certainty that at least some of these patients did not have a larval nephritis prior to the pregnancy in question. If, however, this process existed, it must have been extremely mild inasmuch as it produced no signs prior to the seventh month. Indeed, several of the women had been under our observation in previous pregnancies which were entirely normal. Consequently, it seems very probable that they owe their nephritis directly to the toxemic condition, which developed during the present pregnancy. In any event, one can say with certainty that any renal condition hitherto existing had become markedly aggravated by the pregnancy. In a number of instances the blood pressure six weeks postpartum was much higher than at any time prior to delivery.

We wish to point out that the custom of classifying a given toxemia by the blood pressure and urine findings during the course of pregnancy or even at the time of discharge from the hospital early in the puerperium is fallacious. Our observations show that many patients with an undoubted nephritis will have a normal pressure and negative urine after delivery and two weeks' rest in bed, while on the other hand, some women who leave the hospital after a toxemic attack with hypertension and albuminuria will later return entirely to normal.

Finally, it seems apparent that not only must we view every case of apparently mild toxemia with apprehension, since it may eventuate in an unexpected attack of eclampsia, but we must also be prepared to find at least an eighth of them several months later suffering from a definite chronic nephritis, which, however, is usually mild.

(For discussion, see page 441.)

EROSION, LEUCOPLAKIA AND THE COLPOSCOPE IN RELATION TO CARCINOMA OF THE CERVIX*

BY EMIL RIES, M.D., CHICAGO, ILL.

THE study of erosion and leucoplakia of the cervix has entered upon a new period since the introduction of the colposcope,† which is the invention of Professor H. Hinselmann of Hamburg. It is constructed so as to give an enlarged stereoscopic picture. The instrument for use in the office affords enlargement up to tenfold. A special construction for purposes of investigation supplies enlargement up to forty. The instrument is built for binocular use. It is mounted on a metal stand which permits of easy movement in every direction. Its manipulation is simple. (Fig. 1.)

The results of Hinselmann's work with the colposcope should have been published long ago as an introduction for the use of the profession. The difficulty which is causing the delay lies in the fact that the findings in the colposcope are practically impossible of rendition in black and white. Only reproductions in colors can give an adequate idea of what the colposcope reveals and the undertaking of a much needed atlas in colors has met with prohibitive financial difficulties. The only good reproductions of some of the pictures which Prof.

^{*}Read before the Chicago Gynecological Society, April 17, 1931. †Colposcopes are manufactured by E. Leitz, Wetzlar.

Hinselmann's artist has painted are found at present in Hinselmann's chapter on "Etiology of Carcinoma of the Uterus," in Stoeckel's *Handbuch der Gynaekologie*, Volume 6.

EROSION

Erosion much more than leucoplakia has been in the minds of gynecologists as a condition associated with carcinoma. Its descriptions for many years have been fairly uniform. The name is explained by



Fig. 1

the development of our knowledge of erosion. In the primitive period of gynecology, when the speculum furnished the closest means of study of the cervix, the early observers believed the red areas to be raw. The name of erosion expressed their concept of an area deprived of the normal surface layer. When Ruge, Veit, later R. Meyer studied the microscopic appearance of these areas it became evident that there was no loss of tissue, but a change from the normal stratified

epithelium to the columnar type. The name of erosion was therefore corrected into pseudoerosion, but the usage of decades has been to call the condition erosion with the tacit understanding that it is not a condition of tissue defect.

The embryologic study then revealed the fact that columnar and stratified epithelium are not definitely circumscribed to definite areas from the beginning throughout life, but that they are in a more or less constant change from one to the other and that this change can go on throughout life.

This process may lead to appearances of the portio which on inspection arouse the suspicion of carcinoma. Exploratory excision for microscopic investigation then is commonly used to decide the question. The decision often is easy, but there are many cases in which the irregularly arranged epithelium may necessitate considerable study and cause disagreement among investigators. As erosions are studied in the colposcope, their various appearances must be correlated with the microscopic findings on sections from exploratory excisions. If we compare constantly the colposcopic findings with the microscopic findings, we may learn to differentiate benign erosion and carcinoma with the colposcope without exploratory excision. Since there is a group of surgeons who object to the exploratory excision as a possible cause of metastatic growth, such an achievement would be most desirable.

In another way we have found the colposcope helpful, namely in guiding the treatment of erosions. The cautery treatment which at present may be called paramount, is handled most successfully under colposcope control. Not only is this true as to the extent of the erosion which is to undergo treatment, but especially in the early detection of areas in which repetition of the treatment is needed. In many cases which on macroscopic inspection appeared well skinned over, extremely minute red areas have been discovered by the colposcope in the midst of the newly formed stratified epithelium. On further watching these red spots now and then have developed into new areas of erosions. By timely discovery and treatment the course of the erosions which in our hands had not by any means progressed as steadily to complete healing as some reports would lead us to expect, is guided to the desired end.

When the erosion is healed completely, it presents the picture of the transformation zone as Hinselmann describes it, a picture with which the colposcope makes us familiar in a way which no ordinary examination with hand or speculum can supply. To reduce the area of erosion to the condition of the smooth transformation zone means to cure the erosion.

LEUCOPLAKIA

While erosion is a constant danger sign for cancer at its earliest stage, leucoplakia means nothing to most observers. Very few have ever seen one and fewer still have had the opportunity to see it develop into carcinoma. It cannot be diagnosed by palpation and is easily overlooked in ordinary speculum examination. In fact, Hinselmann states that he had never seen a case himself before he used the colposcope, while in his report of June, 1929, he has accumulated 110 cases. In my own experience which is less than one year old, I have seen now two cases of leucoplakia, but had never before discovered one on examination of patients without the aid of the colposcope.

The scanty literature on leucoplakia is full of contradictions and the subject evidently is in need of considerable general attention before it can be settled definitely. It may be expected that the use of the colposcope is of prime importance in this movement, as it promises a greater number of cases discovered within a short time than the whole previous history of gynecology has supplied.

Leucoplakia is of sinister importance because of its connection with the growth of carcinoma. In six cases in the literature, development of carcinoma has been observed on the basis of leucoplakias followed for considerable periods of time. Whether this change into carcinoma is the universal and unavoidable outcome of every leucoplakia is unknown so far. Nor is the immediate future likely to present us with a great number of additional cases of such cancer development, as it is not to be expected that in our present state of knowledge many will be coldly scientific enough to watch a leucoplakia grow for years instead of promptly removing it to prevent further developments.

Leucoplakia appears in the colposcope as a white area, single or multiple, on the portio vaginalis or in the vagina or in the cervical canal, if the latter is open to inspection in consequence of laceration. The area is smooth. When an attempt is made to wipe if off, the underlying tissue looks different from the surrounding area. In a day or two the patch recurs.

To obtain the leucoplakic area of the portio for microscopic examination does not require amputation of the entire cervix. But it must be remembered that if a piece larger than the leucoplakia is removed, the lesion is impossible of recognition on the dead specimen, especially when it has been hardened in formalin. In order to obtain sections of the leucoplakia alone without cutting the whole specimen, it is necessary to have the exact location defined in memory or, as I have found helpful, by placing finest sutures through the superficial tissue at two opposite points beyond the leucoplakia, but inside the area to be excised.

Hinselmann has examined a considerable number of excised leucoplakic patches in a most thorough manner in serial sections and has given minute descriptions of his findings. The two most impressive features on microscopic examination which stand out even without serial sections, are to be found, one throughout the leucoplakia and the other one at its border. The cells of the leucoplakia are packed densely, they take deeper stain in their protoplasm and in their nuclei, they are more irregularly arranged than in the normal stratified epithelium. Their basal layer is different from the normal basal layer in shape and staining quality. Protoplasmic bridges between the cells of the malpighian layer are less frequent and less pronounced. At the border of the leucoplakia there is a complete change which surprises the observer by its abruptness in a sharp, usually perfectly vertical line extending from the base to the surface. In the leucoplakia the very last basal cell toward the normal tissue produces a totally different generation of cells from those starting out from the first and all other basal layer cells of the normal epithelium.

From the leucoplakia masses of abnormal epithelium protrude into the connective tissue underneath to a varying depth. The surface always remains flat. But the growth downward can extend so far and become so irregular in its outline that a first glance invites the diagnosis of carcinoma. Considerable discussion has arisen about this feature. What one author calls simply atypical growth, another unhesitatingly qualifies as carcinoma. Hinselmann has gone to the trouble of rebuilding serial sections by the modeling method into three-dimensional representations of his most advanced cases of leucoplakia and these models leave little doubt as to their desperate similarity to small carcinomas.

Hinselmann argues that all leucoplakias observed for sufficient time have developed carcinoma (the 6 cases mentioned above). His own advanced cases are practically impossible of differentiation from carcinoma. It appears from the literature that leucoplakia may take years to develop carcinoma. Therefore every leucoplakia must be considered a step in the development of the carcinomatous process.

Hinselmann has observed numerous cases of syphilitic leucoplakia on the portio and their differentiation from the nonsyphilitic is a matter requiring further study. If the clinical and laboratory investigation of the patient with a doubtful leucoplakia indicates syphilitic infection, the therapeutic test may be employed. Hinselmann, however, reports a case of leucoplakia in a syphilitic woman recurring after careful antisyphilitic treatment.

CARCINOMATOUS SURFACE COATING

Pronai, Schauenstein, Kermauner, Schottlaender, von Franqué, Lahm and others have described a condition which they call "carcinomatous surface coating" (Belag, in German). It occurs in two forms, probably different stages of the same process. In one the typical carcinomatous tumor with invasion of the deep layers is more or less surrounded by an area in which the surface epithelium is replaced by a layer of cells which are exactly like the cells of the carcinoma, but do not invade the underlying tissue. These cells end abruptly and without transition toward the normal epithelium. They form therefore a coating in the same way as the frosting on the so-called frosted liver, though of a different composition. In other cases this frosting or coating is the only carcinomatous change in the uterus, but may extend over the entire cavity. Its carcinomatous nature might be considered doubtful, were it not for the fact that more or less lymphatic involvement may accentuate the malignant nature of the process. If any part of such a surface coating produces considerable invasion of the deeper layers of the organ, the condition first mentioned of a typical tumor surrounded by a zone of coating, would be the result.

These surface coatings appear entirely different from the surrounding mucosa if observed in the colposcope. They have been discovered without the colposcope on microscopic examination only. But the colposcope will enable us to diagnose them in the living, if they come within the range of the eye reinforced by the instrument.

ADDITIONAL USES OF THE COLPOSCOPE

Gynecologists generally regret the fact that carcinomas do not reach them as early as they should. By the time the classic symptoms of irregular discharge and hemorrhage lead the patient to the physician and the case is diagnosed from the findings of tumor or ulceration or both as malignant, the process frequently is found to be quite advanced. Carcinomas have been described as early cases, the dimensions of which can be expressed in several centimeters, the smallest one known being 1 by 0.75.

With a ten power enlargement such as the colposcope affords, it is certain that smaller carcinomas can be found. A tumor only one millimeter in its greatest dimension of surface would appear of one centimeter size. While it might be overlooked in an ordinary speculum examination, it cannot fail to strike the eye of the examiner as something abnormal inviting further investigation. The principal advantage of the instrument is that changes in the surface are so minute that they cannot be felt and can easily be overlooked in the ordinary speculum examination, but become plainly visible in the colposcope.

There exists a gap in our knowledge of carcinoma of the portio between the smallest carcinoma detected by the microscope alone and the distinct tumor which is commonly seen. Naked-eye observations of the stages between these two are lacking. From the work of Kermauner and Schottlaender it is evident that at the present time carcinomas are constantly overlooked. They examined microscopically the cervix in 400 uteri which had been removed for causes other than carcinoma, such as fibroid, metropathy, etc. In these they found carcinoma in 2 per cent of the portios which in the preoperative diagnosis had escaped detection. No colposcopic examination of these cases before operation is reported. Routine examination of all cases preparing for hysterectomy should link up the colposcopic findings with the microscopically small carcinoma which at present is overlooked.

There is a period of growth of carcinoma between this stage shown by Kermauner and Schottlaender and the stage which is represented by the smallest visible or palpable tumor. This intermediate stage is unknown in its macroscopic appearance and possibly only represented by certain observations of carcinomas removed in exploratory excisions. These observations concern cases in which the carcinoma was so small that the exploratory excision comprised all of it and no further carcinoma could be found in the organ removed completely. Frankl has discussed these very early cases as to their microscopic pictures, but there are no descriptions in the literature of their macroscopic or colposcopic appearance. Here again future work with the colposcope should widen diagnostic possibilities.

GENERAL USE OF THE COLPOSCOPE

In order to lessen the deplorable carcinoma mortality various propositions have been made in the direction of preventive surgery, such as suture of all lacerations of the cervix, amputation of the cervix, or even vaginal hysterectomy on every woman of carcinoma age. All of these so-called protective methods fail to reach the bulk of carcinoma candidates, because they involve an operation. They furthermore appear largely unnecessary, because they would remove many organs which never would have developed carcinoma.

But it would be entirely rational to invite all women to regular colposcopic examinations. As these are simple and painless and require little time, they ought to be consented to readily and repeatedly. The colposcope would then lead to the discovery of carcinomas at such early stages that extensive operations would not be needed. The fight against uterine cancer of which carcinoma of the portio represents a large proportion could thus be waged with increased chances of success.

The fundamental difficulty to be overcome has always been the indifference of the patients. It is necessary to acquaint them again and again with the risks of tumor development, but it is also necessary to inform them of simple improvements in the means of diagnosis in order to break down their fears of painful procedures and interest them in ways and means of protecting themselves. A colposcopic examination must come to be part of every periodic health examination, of every examination for life insurance and should be as familiar and routine as an uranalysis and a blood examination.

REFERENCES

(For discussion, see page 451.)

Pronai: Arch. f. Gynäk. 89: 1909.
 Schauenstein: Gynäk. Rundschau.
 1907.
 Von Franqué: Stoeckel's Handbook of Gynaecology 6: 1930.
 Lahm in Halban: Biologie des Weibes 4: 1927.
 Frankl: Zentralbl. f. Gynäk.
 1921.
 Kermauner-Schottlaender in Halban: Biologie des Weibes 4: 1927.

POSTERIOR OCCIPUT PRESENTATION*

Analytical Review of Posterior Occiput Presentations Occurring in 1,000 Consecutive Deliveries at the Evanston Hospital

BY R. A. SCOTT, M.D., F.A.C.S., EVANSTON, ILL.

(From the Department of Obstetrics and Gynecology of the Evanston Hospital)

IT HAS been customary from time to time in the obstetric department of the Evanston Hospital to review the histories covering certain types of delivery. Such analytical reviews have been instructive and beneficial, for in retrospect our method of treatment is often an improvement over the actual methods used.

The number of occipitoposterior presentations occurring in the 1,000 consecutive cases in the period from November, 1928 to January, 1930 inclusive was 144, an incidence of 14.04 per cent. These we have placed in three groups:

- Group 1. Posterior occipitopresentation, delivered in the posterior position.
- Group 2. Posterior occipitopresentation, rotating spontaneously to anterior position.
- Group 3. Posterior occipitopresentation, rotated manually to an anterior position.

Group 1.—Fifty (50) or 34.7 per cent of the total number of cases were delivered in the posterior position. As might be expected there were only 10 primiparae, the remaining 40 being multiparae. All patients were at term. The duration of labor varied from one hour and fifty-two minutes to thirty-three hours and fifty minutes; the average length of labor being seven hours and thirty-seven minutes. The length of the first stage varied from one hour and forty minutes to thirty-three hours and forty minutes, with an average length of seven hours and twenty-four minutes. The second stage had a variation of ten minutes to four hours and fifteen minutes with an average duration of forty-one minutes. Thirty-six delivered spontaneously, 11 with low forceps and 3 with mid forceps. Only a small percentage of this group received any sedative during the first stage. There was no maternal or fetal mortality.

Group 2.—Posterior occiput presentations rotating spontaneously to an anterior position, numbered 43, or 29.9 per cent of the total number of cases. All of these patients were at term. There were 20 primiparae, about double the number in group one, and 23 multiparae.

^{*}Read before the Central Association of Obstetricians and Gynecologists, Excelsior Springs, October 10, 1930.

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The hours of labor varied from two hours and forty-eight minutes to twenty-seven hours and thirty-three minutes, an average duration of eleven hours and thirty-six minutes.

The first stage varied from two hours and ten minutes to twentyseven hours and twenty-five minutes, an average first stage of ten hours and fifty minutes, an increased average of about three hours over that of group one. The second stage varied from ten minutes to three hours and three minutes, giving an average second stage of fifty-two minutes as compared with forty-one minutes in group one. In this group an estimate was made of the time the head remained in the posterior position, before the spontaneous anterior rotation. The time varied from two hours and ten minutes to twenty-seven hours and fifty minutes; with an average time of eleven hours and twentyfour minutes. This is a reasonably accurate estimate because the interns are instructed to see the patient every half hour or oftener if necessary and rectal examinations are made if there is an increased frequency or any change in the character of the pains. Although to some it may appear too long a period to allow the head to remain in a posterior position, the resulting absence of either maternal or fetal mortality in this group rewarded our conservatism. Thirty-two delivered spontaneously. Ten with low forceps and one with mid forceps.

Group 3.—Posterior presentations which were rotated manually to an anterior position (one exception being a Scanzonian maneuver) numbered 51, or 35.4 per cent of the total number of cases, 37 primiparae and 14 multiparae. In this group we thought it unnecessary to note the length of time in the first and second stage of labor because the time the head was allowed to remain in the posterior occiput position before interference is the important point to consider. The elapsed time in each instance was just a few minutes less than the total hours of labor. The shortest time elapsed was fifty minutes and the longest thirty-seven and one-half hours, or an average time of twelve hours and twenty-eight minutes. Full dilatation was completed normally in all but 3 instances. In one of these three Duehrssen incisions were made, and in two, complete dilatation was produced manually.

Period of complete dilatation before attempted delivery was also noted. In 23 instances, delivery was made immediately after complete dilatation. In 28 cases, the time ranged from fifteen minutes to three hours and five minutes, an average time of forty-seven minutes before any interference was instituted.

The indications for immediate delivery or delay, were:

In the ease of the mother

- 1. Amount of exhaustion
- 2. Type and frequency of labor pains and degree of effacement and dilatation

In the case of the baby

- 1. Rate and strength of fetal heart
- 2. Degree and rapidity of descent of head
- 3. Ratio between head and pelvis

In all instances except one, a Scanzoni operation, the head was rotated to an anterior position manually. In every instance forceps were applied and delivery attempted. Thirty-five in this group were forceps deliveries; 26 low forceps, 8 mid forceps and 1 high forceps, the remaining 16 were delivered by version and extraction. No mothers were lost, but three babies died as a result of the version and extraction manipulation. One lived a few minutes and the other two were stillborn. The fetal heart was audible until the delivery started. The postmortem examination on these babies revealed brain hemorrhage, traumatic in origin.

In 13 cases cervical lacerations were found, and in 1 case Duchrssen incisions had been made. The remaining 37 had no cervical tears.

DISCUSSION

The discussion of these cases must necessarily be the author's personal opinion and he therefore craves your kind indulgence,

Group 1 in which the patients delivered in the posterior position show a surprisingly short average labor of seven hours and thirty-three minutes. It being the general impression that such a type of delivery is accomplished only after long hours of labor, this low average, in part is due, I am sure to our routine use of nitrous oxide and ethylene gas for analgesia in the second stage of labor. A specific instance showing the importance of hospitalization in obstetric cases.

Group 2 in which anterior rotation was spontaneous, numbered 43, or 29.9 per cent of the total number of cases. This is a very satisfactory percentage for it is this type of case that demands sound obstetric judgment, and requires experience and training for its proper management.

In group 3, where interference is indicated there are in most cases definite symptoms relating to mother or fetus that aid one's judgment. The important consideration is, with what type of interference to proceed in a given case. The infant mortality rate of 5.88 per cent (3 out of 51 cases) is a little high, showing either an error in judgment, or lack of skill in the delivery.

A. Concerning a possible error in judgment in this procedure.—Perhaps the labor was allowed to proceed to the detriment of the fetal heart strength, or a disproportion between fetal head and pelvic outlet escaped notice.

B. Concerning lack of skill at this point.—Perhaps the head was not rotated to the anterior position, or there was a possible faulty application of forceps, or there was too much traction with the forceps, or in the case of version and extraction, a brain injury to the child was

inflicted because the operator was in too much of a hurry in delivering the after-coming head.

The author has occasionally, in the case of a small fetus delivered a persistent occipitoposterior by version and extraction without any attempt at manual rotation. When the head is small and the bone plates in the baby's skull are widely separated, I think it a little safer procedure than the use of forceps. If we all had the skill of a Potter some of our version and extractions might be more successful. Although many obstetricians apply forceps to the after-coming head as a routine measure, the staff at the Evanston Hospital delivers more cases without than with the aid of forceps. We have had good results with the Piper forceps.

Cesarean section is correctly indicated in persistent posterior occiput presentation when the trial of labor has been sufficient and dilatation has not progressed to the point where its completion can be executed. This is particularly the case in the so-called borderline type of contracted pelves.

The author would like to state that he found Keielland's forceps, because of their shape and length, very satisfactory if applied in like manner to other forceps to the anteriorly rotated head. We have not had much success with these forceps when using them in the manner prescribed by their inventor.

PROLAPSED UMBILICAL CORD*

AN ANALYSIS OF ONE HUNDRED CASES

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WE MAY consider prolapsed cord a condition in which that structure has left its normal site and has taken a position compromising the life of the fetus. According to its position we may classify this entity as follows: (1) occult or concealed, (2) presenting, and (3) prolapsed.

The statistics of prolapsed cord herewith presented are based on the records of 100 consecutive cases treated at Harlem Hospital in New York during the years 1915 to 1927 on the services of George L. Brodhead and Fred A. Kassebohm, and represent the combined work of ten members of the visiting staff and a number of interns.

Frequency of Prolapsed Cord.—In 16,942 consecutive deliveries there occurred 100 cases of prolapsed cord giving a frequency of one in 169 deliveries. This figure tallies with the ratios reported in several of the recent series, as noted in Table I. The average frequency is about

^{*}Read before the Section of Obstetrics and Gynecology, New York Academy of Medicine, New York City, November, 1930.

1:137. DeLee reports a frequency of 1:400. On the other hand, Dietrich and Schweitzer report a ratio of 1:85:88. This increased frequency is reported by these authors as due to the prevalence of rickets in their community.

TABLE I. INCIDENCE OF PROLAPSED CORD

AUTHO	R	NO. DELIVERIES	NO. PROLAPSE	
Stowe	1907	7,900	48	1:164
Dietrich	1908	26,743	312	1:85
Knapp	1912	68,000	624	1:189
Makouski	1912	13,059	85	1:165
E. Zweifel	1912	10,000	66	1:151
Roth	1919	25,333	165	1:153
Halter	1920	90,468	894	1:101
Schweitzer	1922	18,934	214	1:88

Position and Presentation.—Abnormal position and abnormal presentation at birth have been frequently referred to as a primary cause of prolapsed cord. However, in the present series, 59 cases of prolapsed cord occurred in vertex presentation, 23 in breech, and 18 in transverse presentation. The incidence of occurrence predominates in transverse cases. As indicated in Table II, prolapsed cord occurs about once in every 200 cases of vertex presentation, about 6 times in 100 breech cases, and about 10 times in every 100 transverse presentations.

TABLE II. INCIDENCE OF PROLAPSED CORD AS TO PRESENTATION

	PRESENTATION		
COMPILER	VERTEX PER CENT	BREECH PER CENT	TRANSVERSE PER CENT
Cunz	1.01	5.51	12.2
Scanzoni	0.35	4.37	7.28
Hecker	0.68	9.09	5.81
Gusserrow	0.76	5.81	14.29
Zweifel	0.41	5+	10.3

Period of Gestation.—In the present series there were 71 cases of prolapsed cord at full term, 17 at eight, and 12 at seven months of gestation. From the point of view of parity, prolapsed cord occurred in 26 primiparae and 74 multiparae. Prolapsed cord is about three times more frequent in multiparae than in primiparae, and the incidence of prolapsed cord increases with the added parity.

Previous Labors.—Of the 74 multiparae, 64 gave histories of previous normal labors. In the remaining 10 cases, 2 patients had cesarean sections for contracted pelves, 6 were delivered by forceps, and one had a breech presentation. The previous labor of one patient was unknown. Stowe reported 12 cases with previous obstetric complications in his series of 51 cases, two of whom had a previous prolapsed cord. He also reported a case which had a total of three deliveries, all complicated by prolapsed cord.

Degree of Cervical Dilatation.—In 75 patients the cervix was fully or almost fully dilated when they were first seen. In the remaining 25 patients the dilatation was from 1 to 4 fingers.

The Relationship Between Prolapsed Cord and Membranes.—In this series, 70 of the patients were admitted to the hospital with membranes ruptured and the cord prolapsed. The remaining 30 patients were admitted with unruptured membranes. The cord was felt presenting through the membranes in 5 instances. In the remaining 25 cases the cord was not felt, but when the membranes ruptured, the cord prolapsed.

Fetal Heart and Cord Pulsation.—We noted that there were 11 patients with normal fetal heart sounds but not cord pulsation, 7 of whom gave birth to a living baby. There were 2 patients in whom no fetal heart could be heard despite pulsating cord, and in one instance a living child was born. Further there were 2 with absent fetal heart sounds and cord pulsations, and both were delivered of a living child.

Deformities of the Pelvis and Other Complications.—Deformed pelvis is reported to be the most common cause of prolapsed cord. Hildebrandt, Von Winckel, Engelman, Gusserow and others reported from 33 to 45 per cent of cases with prolapsed cord in contracted pelves, whereas in our series 17 patients were found to have contracted pelves, about 17.5 per cent of the total number of cases. There was an added complication of placenta previa in 5 instances. In 5 other cases an accidental hemorrhage had occurred, and there was one case of hydramnios. Placenta previa per se predisposes to prolapsed cord in two ways: first, the placenta by its low implantation displaces the cord downward; and second, the presence of the placenta in the lower uterine segment may interfere with the engagement of the presenting part.

Bagging and the Occurrence of Prolapsed Cord.—The introduction of a bag to induce labor or hasten cervical dilatation is frequently a factor in the production of prolapsed cord. The larger the bag inserted, the greater the displacement of the presenting part. Schweitzer reported 214 cases of prolapsed cord, 17 of which followed the insertion of a bag. In our series, 7 cases of prolapsed cord followed the introduction of a bag.

Thus it will be seen that the fetal mortality is relatively greater in transverse presentation and relatively lower in footling presentations.

TABLE III. GROSS FETAL MORTALITY = 63 PER CENT

PRESENTATION	NO. OF CASES	NO. OF STILLBIRTHS	PER CENT OF FETAL MORTALITY
Transverse	18	13	72.2
Vertex	59	40	67.7
Breech	11	6	54.5
Footling	. 12	4	33.3

It is strange, however, that the fetal mortality in transverse presentations, where the pressure on the cord is commonly assumed to be slight, is higher than in vertex presentations where cord compression is increased.

There were 34 fetal deaths before admission. Therefore, in order to estimate the value of the treatment administered, only those patients who were admitted with a living fetus must be considered. There were 66 such patients, 37 of whom were delivered of living babies, and 29 of stillbirths, giving a fetal mortality of 43.9 per cent. (See Tables IV and V.)

TABLE IV. FETAL MORTALITY PRIOR TO ADMISSION

PRESENTATION	NO. OF CASES	NO. OF FETAL DEATHS BEFORE ADMISSION	PER CENT OF FETAL MORTALITY	
Transverse	18	11	61.1	
Footling	12	4	33.3	
Breech	11 3		27.2	
Vertex	59	16	27.1	

Table V. Fetal Mortality After Admission =43.9 Per Cent

PRESENTATION	NO. OF CASES	NO. OF STILLBIRTHS	PER CENT OF FETAL MORTALITY 55,5	
Vertex	43	24		
Breech	8	3	37.4	
Transverse	7	2	28.5	
Footling	8	0	0	

There are, of course, added factors which increase the fetal mortality, namely, contracted pelvis, accidental hemorrhage, placenta previa and prematurity. It is of interest to note that in 8 cases with contracted pelves, vertex presentations and prolapsed cord, there were 7 stillbirths; and in 3 instances with contracted pelves and breech presentations, there were no stillbirths.

Cervical Dilatation and Fetal Mortality.—Of 14 patients in whom the cervix was dilated 4 fingers or less when first seen, there were 8 stillbirths, giving a fetal mortality of 57.1 per cent. There were 52 patients who were from 4 fingers to full dilatation when first seen, and of these, there were 21 stillbirths, giving a fetal mortality of 40.3 per cent.

A further analysis of our fetal mortality shows that in 18 transverse presentations, 11 babies died prior to hospitalization. Of the 7 cases admitted, only 2 were lost. Likewise in footling presentations, of which there were 12, 4 babies died prior to admission. In the remaining 8 cases none were lost. It is interesting to note that while transverse and footling cases present a high fetal mortality prior to hospitalization, the results of therapy were gratifying. In vertex presentation the results were less successful since in 43 cases admitted with living fetuses, 24 babies were lost.

Maternal Mortality.—There were no maternal deaths in this series which could be ascribed directly to the prolapsed cord and the treatment thereof. Two mothers, however, died, one as a result of a premature separation of the placenta and the other from sepsis, death occurring two weeks after delivery. This patient was admitted with a history of previous interference.

In conclusion we may state that despite the various therapeutic measures available, prolapsed cord still remains a serious complication with a very discouraging fetal mortality.

545 WEST END AVENUE.

OBSERVATIONS ON THE USE OF SPINAL ANESTHESIA IN ABDOMINAL OBSTETRIC OPERATIONS*

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PREGNANCY, whether or not we view it as a physiologic state, is all too often a complicating factor in preexisting organic disease of the individual. Quite as important and serious are the metabolic and organic disturbances, which occur with, and are directly attributable to, human gestation.

It all too frequently happens, when certain of these conditions apply, that the life or health of the mother is endangered. This situation presumes a risk to the viable child equally as great as that of the mother. If operative termination of the pregnancy is indicated, the necessity for obviating all possible damage due to the anesthetic must be considered.

The safety of the patient is always a paramount consideration. Therefore, the employment of any anesthetic agent which increases the risk to the patient can be justified only by definite compensating advantages which accrue through its use.

In certain of the complications of pregnancy, spinal anesthesia may be employed to good advantage. It is the purpose of the present discussion to attempt an evaluation of its advantages and disadvantages under the conditions mentioned above.

The early use of this method of anesthesia in obstetrics is credited to Kreis¹ (1900). Shortly thereafter it was used for the same purpose by Doleris, Marx, Dupaigne, and others.²

Cocaine, which was used at this time, was so toxic that the procedure was early brought into disrepute. The less toxic drugs, stovaine and novocaine, have since

^{*}Read before the Boston Obstetrical Society, October 21, 1930.

been developed, and are now generally employed. The latter preparation is used almost exclusively in this country. More recently Brindeau³ and Delmas⁴ in France, and Krause⁵ in Germany, have used lumbar anesthesia in obstetrics over a considerable period with satisfactory results.

Certain developments in the technic of spinal anesthesia have caused a revival of interest in it during the past few years. The use of ephedrine, improved lumbar puncture technic and the development of anesthetic solutions of low diffusibility have been the chief advances.

The introduction of the use of ephedrine with lumbar anesthesia is credited to Ockerblad and Dillon⁶ (1927) and represents a real advance. This drug is a powerful peripheral vasoconstricting agent, which acts on the sympathetic system and counteracts or diminishes the vascular depression which formerly in spinal anesthesia was much feared. The duration of its action is sufficient for the average operation and as Sise⁷ has pointed out, it is more effective in preventing blood pressure fall than in raising it, once the drop has occurred.

Improvement in lumbar puncture technic has consisted largely in the use of smaller needles with points designed to produce minimal trauma to the dura. The severe postanesthetic headache is no longer a common complication.

There has also been a revival in the use of novocaine solutions of specific gravities either higher or lower than that of the spinal fluid. Pitkin⁸ has added to these a stable starch which prevents rapid diffusion of the novocaine with the spinal fluid until fixation of the drug by nerve tissue has occurred.

This solution, known as "Spinocaine," is of lower specific gravity than the spinal fluid and is well suited to anesthesia involving the upper and lower abdomen. Because of the differential specific gravities of the solution and the spinal fluid, the patient must be kept in some degree of Trendelenburg position until the novocaine mixture has become fixed. Since the majority of abdominal obstetric operations preferably are done with the patient in this position, spinocaine presents no objectionable features on this account.

The use of novocaine (procaine) crystals dissolved in spinal fluid and injected into the subarachnoid space still constitutes, according to Labat, one of the most simple, safe and sound methods of inducing lumbar anesthesia. When novocaine solution is injected into the subarachnoid space a combination occurs between the solution and the anterior and posterior roots in contact with the drug, resulting in interruption of the nerve conductivity.

The sympathetic nervous system controls vasoconstriction and has intimate connections with the spinal roots by way of the rami communicantes. Therefore, the higher the spinal roots are involved, the higher the level of paralysis of the sympathetic chain. Any large involvement of this system will cause dilatation of the splanchnic blood vessels with resulting diminution of blood pressure. Fortunately, in abdominal obstetric operations, a level of anesthesia slightly above the umbilicus is adequate. It is unusual to have nausea, vomiting, or extreme blood pressure fall with anesthesia at this level.

On the basis of numerous spinal anesthesias in pregnant women, and of experiments on pregnant rabbits, Ducuring¹⁰ concluded that the human pregnant uterus behaves under spinal anesthesia as does the pregnant uterus in rabbits after complete section of the lumbar part of the spinal cord. It has been frequently observed in cesarean sections under spinal anesthesia, that immediately after the extraction of the child the uterine body contracts firmly and remains contracted, while the lower uterine segment and vagina are relaxed.^{3, 11} The author has yet to see a case of postoperative atony of the uterus following subarachnoid block. From this standpoint, it is ideal for the performance of cesarean section, especially of the low cervical type.

The diminished hemorrhage noted during operation under this anesthesia is due to lowered blood pressure and implies that hemostasis must be carefully effected in order to prevent postoperative oozing and hematoma formation.

The excellent relaxation of the abdominal walls, the contracted intestines, and the facility with which operative procedures may be accomplished, have been sufficiently extolled in recent surgical literature.

No one who has had experience with this method can fail to be impressed by the diminished postoperative discomfort experienced by these patients. They are able to take food early and marked distention is seldom seen. These observations bear out the statement of Babcock¹² that "when properly employed, no other anesthetic of equal range leaves so few sequelae."

The greatest disadvantage of spinal anesthesia is inherent in the method, i.e., that the total dose of the drug is injected at one time, and any untoward reaction of the patient cannot be treated by its removal. Failure of induction occurs in 5 to 6 per cent of cases according to De Takats.¹³ It is due in the majority of cases either to extradural injection, or leakage of the drug. The disadvantages of the relatively short duration of anesthesia do not obtain in abdominal obstetric operations because these procedures may be accomplished within the time limit of anesthesia with a minimal or average dose.

The one complication of spinal anesthesia most feared, is that of vascular depression followed by respiratory failure. The histories of fatal cases show that the most serious type of respiratory collapse is that occurring in the first few minutes following anesthesia. It is the most difficult with which to deal and according to Labat, 14 is due to heavy dosage or poor induction technic.

Respiratory failure may occur any time during the operation especially the first thirty minutes. Its occurrence is preceded by fall in blood pressure, and the symptoms associated are change in respiratory rhythm, pallor or cyanosis and mental torpor. Sise⁷ has called attention to the extreme susceptibility of these patients to anoxemia. If these changes are recognized, early treatment is most effective and satisfactory.

This means that with spinal anesthesia, the anesthetist must not only know the physiologic actions of the drug and the correct technic for its use, but he must anticipate and recognize all untoward reactions of the patient and be in a position to begin immediate treatment. For the details of treatment of respiratory failure and the minor complications of spinal anesthesia, the excellent reports of Sise,⁷ Labat⁹ and Babcock¹² should be consulted.

It has been suggested that the presence of pregnancy may increase the risk for the patient in abdominal operations under spinal anesthesia. Despite various explanations, which have been advanced for this possibility, the explanation of Babcock¹⁵ seems a most rational one. He says, ''It is my impression, that owing to the limited action of the diaphragm from the abdominal distention, the danger of spinal anesthesia is somewhat greater in the latter months of pregnancy.'' To counteract such increased risk, means that the dosage of the drug must be kept at a minimum; the level of anesthesia must be kept low; and the respirations closely observed.

If the mortality statistics tell us anything, it is that indiscriminate use of spinal anesthesia is a dangerous procedure but that used discreetly it is a method of great value. Tendler¹⁶ has collected from the literature 326,910 spinal inductions with 80 deaths. This means a ratio of one death in 4,086 cases. Babcock,¹⁵ who has performed over 20,000 spinal inductions, considers that this anesthetic has a mortality of about one to 500 when used indiscriminately and without skilled care, and less than one to 10,000 when used under the best conditions. Sise⁷ has shown what has resulted from the general enthusiastic adoption of this method in

our own community. He concluded that the ratio of mortality under these circumstances was approximately one per 100 cases.

In Table I are listed recent series of cesarean sections under spinal anesthesia, with deaths attributed to this method.

TABLE I

AUTHOR	DRUG	CESAREAN SECTIONS	DEATHS DUE TO ANESTHETIC
Brindeau ³ (1926)	Stovaine	102	2*
1 1	Novocaine		
Brindeau ¹⁷ (1928)	Stovaine	60	0
	Novocaine		
Friedman ¹⁸ (1926)	Tropacocaine	100	0
Astley ¹⁹ (1927)	*	13	0
Young ²⁰ (1929)		40	0
Johnson ²¹ (1930)	Novocaine	25	0
		340	

^{*}Includes 132 pelvic operative deliveries.

It must be remembered that spinal anesthesia has not been extensively used in obstetric clinics, and that its use in many cases has been confined to patients regarded as poor risks. The recent series reported from any one clinic, where this method of anesthesia was used, are necessarily small as compared with the larger surgical series. Also the drug used, the dosage and the technic of induction have varied greatly. These are important considerations in attempting to compare results.

Spinal anesthesia may be used in abdominal obstetric operations, with certain exceptions, in those cases in which general inhalation anesthesia is contraindicated, or would add to the gravity of the underlying pathology. Babcock^{12, 15} has demonstrated through long experience that this method must be selective and that it is unsuited for patients in poor physical condition. Careful choice of the patient risk is more important than any other part of the procedure. Until further evidence of the safety of spinal anesthesia has accumulated, its routine use in operative obstetries should be discouraged. Local infiltration anesthesia has been advocated by Irving,²² DeLee²³ and others, for these same conditions. There is no doubt that local infiltration anesthesia carries less risk, but on the other hand, its induction is tedious, time consuming, and in nervous and apprehensive patients, especially, it constitutes an unsatisfactory anesthetic. After a limited but definite experience with both, the preference of the author is for spinal anesthesia when there is reasonable indication for its use.

In preeclampsia, which has not responded to treatment, or which is of the fulminating type, cesarean section is, in certain instances, a preferable method of delivery.³¹ From the work of Stander,²⁴ it is evident that in the toxemias of pregnancy, general anesthesia for operative procedures should be replaced by either local infiltration or subarachnoid block. The rapidity with which anesthesia can be induced, and the operation performed, is of real value in the treatment of fulminating preeclampsia. The lumbar puncture diminishes the cerebrospinal fluid pressure, and the fall in blood pressure following spinal anesthesia accomplishes automatically that which we attempt to obtain by symptomatic treatment. Suppression of urine has not been noted, and the ability of the patient to take fluids immediately postoperative is important. Astley,¹⁹ Johnson,²¹ and Young²⁰ have all reported gratifying results on the use of spinal anesthesia for cesarean section in the late toxemias of pregnancy.

Of the acute diseases of the urinary tract during pregnancy, pyelitis, and

pyelonephritis are most commonly met. If the infections are severe and abdominal operative procedures are indicated, the use of spinal or local infiltration anesthesia is well suited. If careful preoperative preparation by the use of fluids is made, these patients, in general, tolerate spinal anesthesia well.

Nephritic toxemia, or pregnancy complicating a preexisting nephritis, frequently presents a serious obstetric problem. These patients, also, represent in general, serious operative and anesthetic risks. Often it is considered advisable to terminate the pregnancy by the abdominal route.

Under spinal anesthesia the blood pressure fluctuations in this group have been the most extensive. This is presumably due to the peripheral arteriosclerosis associated with the nephritis. No harmful sequelae attributable to these blood pressure changes have been observed. However, it was felt that the margin of safety in these cases, was less than in other groups.

In the nephritic toxemias, it is especially important that fluids be forced preparatory to operation. These patients in many instances, are in poor nutrition and if edema is present, do not seem capable of utilizing this fluid. Fluids up to 3,000 c.c. should be administered in the twenty-four period preceding operation. If the patient will take liquids freely by mouth, palatable drinks containing 10 to 20 per cent glucose supply the fluid in an excellent form. If fluids are not well taken, or if the operation is an emergency, the use of 10 per cent glucose intravenously, or saline by hypodermoclysis will supply the need.

Not only is this preparation designed to produce increased elimination through diseased kidneys, but also to make the patient a better surgical and anesthetic risk. If spinal anesthesia is used, it also provides a supply of fluid for the vascular system, with which to cushion the depressive circulatory changes. In the nephritic toxemic group, I believe that spinal anesthesia should be limited sharply to those patients who present at least a fair surgical risk.

Patients who present high nitrogen retention, evidence of marked sclerosis or visual defect symptoms, in the author's opinion are preferably delivered under local infiltration anesthesia, if abdominal operation is indicated.

Pregnancy complicating essential hypertension is not infrequently seen. Those cases not complicated by definite arteriosclerosis or chronic nephritis are suitable subjects for spinal anesthesia. In those presenting the malignant form, i.e., extreme hypertension and evidence of renal damage, the use of local infiltration anesthesia is most desirable.

Diabetes mellitus is occasionally complicated by pregnancy. The development of large babies under these circumstances is well known. Cephalopelvic disproportion is a common indication for primary cesarean section in this group. Other coexisting organic diseases may demand interruption of the pregnancy and sterilization.

Joslin²⁵ has shown that spinal anesthesia is a useful method in diabetic surgery. In the few diabetic cases in which the author has used this method, it has shown satisfactory results.

The choice of the anesthetic in pregnancy complicating cardiac disease seems no different than the same considerations as applied to general surgery. Sise²⁶ has stated the situation as follows: "Valvular disease without serious myocardial involvement affects the choice of the anesthetic very little if there is not decompensation, and even with mild decompensation, offers surprisingly little difficulty with all forms of anesthesia. In these latter cases, however, any raising of blood pressure is to be avoided. Spinal anesthesia is, therefore, less suitable and regional anesthesia becomes the preferred choice, though spinal anesthesia and the gases with ether may also be employed."

The author has observed two cases of acute myocardial failure in patients with preeclampsia who had presented no previous history or evidence of cardiac disease.

Abdominal delivery of this type of case as well as those of severe congestive failure in pregnancy, he believes, is best effected by the use of local infiltration anesthesia supplemented by inhalation of oxygen-ether mixture if necessary. The use of the heavy spinal solution in cardiac failure has been recommended by Pitkin.²⁷ This necessitates elevation of the head and shoulders during the anesthesia, and is the only position in which these patients are comfortable. If, under these circumstances, however, circulatory depression appears, one of the greatest aids in preventing respiratory failure, i.e., Trendelenburg position, is contraindicated.

The acute and chronic respiratory diseases contraindicate the use of ether by inhalation. The incidence of postoperative pulmonary complications is diminished by the use of spinal or local anesthesia.²⁷ That these forms of anesthesia are superior to nitrous oxide-oxygen or ethylene, in this respect, has not been proved by statistics, but is generally acknowledged.²⁹

In extremely obese patients, lumbar anesthesia presents definite advantages over general inhalation anesthetics. It is well recognized that obesity has frequently associated with it metabolic and organic changes, which make those affected less desirable anesthetic risks. Again, those who present extreme risks should have local infiltration anesthesia, if possible.

In general, the use of spinal anesthesia is contraindicated in conditions in which actual shock or hemorrhage exists or where there is imminent danger of its occurrence. Circulatory depression of varying degrees, cannot accurately be prognosticated with spinal anesthesia, and no method should be used which will tend to accentuate the effects of shock.

In uteroplacental apoplexy, a condition usually accompanied by a toxemia of pregnancy or by chronic nephritis, delivery may be best effected by cesarean section.³¹ Characteristic of this condition is the extreme and progressive shock which follows the separation of the placenta and which is out of all proportion to the uterine hemorrhage. Because there is usually renal involvement, the use of local infiltration anesthesia, with nitrous oxide-oxygen if necessary, seems at present the most desirable. These patients in many instances are desperate risks requiring transfusion either before or during operation, or both. Spinal anesthesia, in my opinion, is definitely contraindicated in this condition.

The presence of placenta previa in which abdominal delivery is indicated does not in itself constitute an indication for the use of spinal anesthesia. Theoretically, the relaxation of the lower uterine segment which occurs would present a real difficulty in the control of hemorrhage after removal of the placenta. Ginglinger and Assovatz³⁰ state that there is no foundation for this fear and report with encouraging results 13 cases of cervical cesarean section for this condition under lumbar anesthesia.

PERSONAL EXPERIENCES

The series of cases in this report consists of 121 abdominal obstetric operations performed under spinal or attempted spinal anesthesia, during the years 1927, 1928, and 1929. Eighty-nine were performed at the Boston Lying-In Hospital. The remaining group consists of private patients of various obstetricians who have kindly made their records available, and of patients in the author's own practice. In the majority of the hospital series, and in all the private cases, the anesthesia has been personally induced or observed.

Preparation of the patient for anesthesia has consisted of the almost routine administration of morphine ($\frac{1}{6}$ gr.) and scopolamine ($\frac{1}{150}$ gr.) hypodermically, one-half hour prior to operation. No unfavor-

able results either to the mother or child have been noted. A few babies were apneic immediately after delivery, but in less percentage than after inhalation ether. If the patient was awake and apprehensive at the time of spinal induction the scopolamine was repeated.

In this series, a routine hypodermic injection of ephedrine sulphate, 0.05 gm. was given approximately five minutes before spinal induction. This dosage has proved satisfactory where only lower abdominal anesthesia was desired. In one instance only was it repeated during the operation, and then in 0.025 gm. amount. Epinephrine was used twice during operations because of extensive blood pressure fall. Novocaine, either in the form of spinocaine (Metz) or novocaine crystals (Metz) has been used exclusively.

Spinocaine was used 107 times. The average dosage represented 0.20 gm. of novocaine. The technic of Pitkin was strictly followed and good results were obtained with this solution. The novocaine in crystal form was used fourteen times with satisfactory results. The dose averaged 0.125 gm. The technic was so similar to that already described by Stout¹³ that for further information the reader is referred to his excellent article.

Seven complete failures, 5 per cent, occurred in this entire series. Intraspinal reinjection of one-half the original dose of the drug produced successful anesthesia in three of these instances. Supplementary anesthesia was necessary twelve times, 7 per cent. In a few instances this was not necessary, except for the psychic effect upon the patient. The operations performed, as well as the indications for anesthesia, are shown in Table II. Of the 82 cesarean sections, 34 were of the classical and 48 of the low cervical type.

TABLE II

INDICATIONS	CESAREAN SECTION	ABDOMINAL STERILIZATION	HYSTERECTOMY OF PREGNANT UTERUS	ABDOMINAL HYSTEROTOMY AND STERILIZA TION
Chronic nephritis	6	3	7	4
Pyelitis	2	1	0	0
Tuberculosis	0	0	0	2
Acute coryza	7	0	0	0
Tuberculosis	1	2	. 1	2
Asthma	2	0	0	0
Cardiac disease	4	1	4	3
Toxemia of pregnancy	17	0	1*	0
Ablatio placentae	4	0	0	0
Pernicious vomiting	0	0	2	2†
Essential hypertension	1	0	0	0
Diabetes mellitus	3	0	0	2
Epilepsy	0	0	1	1
Elective	35	0	0	0
Total	82	7	16	16

^{*}Ruptured Uterus.

It will be noted that 35 cesarean sections were performed under "elective indications." These patients were all normal and used as a control series. In view of the possibility of certain dangers which became apparent after experience with this method, and because it was felt that spinal induction should be limited by strict indication, its use in this type of case was abandoned until further data had accumulated.

The blood pressure fluctuations varied in different patients with identical doses of the drug and a standard technic of administration. This, however, is not surprising when we consider that vascular hypertensive conditions were present in a moderate proportion of these patients. Blood-pressure observations were made at five- to ten-minute intervals during the operations. Large fluctuations in the diastolic pressure were considered more important than in the systolic, and stimulative treatment was carried out on this basis.

A rise in blood pressure immediately after delivery of the child was observed in 80 per cent of the 82 cesarean sections reported. Unfortunately, this postnatal blood pressure elevation seemed to occur with less frequency in those instances in which a large blood pressure fall had already transpired. Since these particular cases presented the worst risks, the practical importance of this phenomenon is greatly vitiated.

The postoperative complications which occurred are tabulated in Table III, and are self-explanatory.

TABLE III

COMPLICATION	NUMBER	PERCENTAGE	REMARKS
Vomiting	3	2 %	One developing intestinal obstruction
Mild distention	21	17 %	
Moderate distention	11	9 %	
Marked distention	3	2 %	One developing intestinal obstruction
Headaches	5	4 %	All responded to sedatives
Meningismus	1	0.8%	Duration three days
Pulmonary edema	2	1.6%	(a) Mild decompensated cardiac dis- ease (b) Preeclampsia
Urinary retention	1	0.8%	Required two catheterizations

In this series of 121 patients, six postoperative deaths occurred. Brief case histories are appended.

Case 1.—Admitted as emergency. Para iii, forty-two years. Diagnosis: utero-placental apoplexy. Blood pressure 190/130 on admission, beginning shock. After administration 2 c.c. of spinocaine, blood pressure dropped to 100/70. Classical cesarean section duration forty minutes. At beginning of operation level of anesthesia 2 inches above umbilieus. During operation, blood pressure continued to drop. Adrenalin hydrochloride 15 minims intravenously, and intravenous saline started. At the end of operation blood pressure was not obtainable. Two transfusions each of 500 c.c. citrated blood given immediately. Patient revived, became conscious, and blood pressure returned to 60 mm. Hg, two hours after operation. Following this, patient relapsed into shock and died four hours from the end of operation.

Case 2.—Para vi. Low cervical cesarean and sterilization performed on patient with severe rheumatic heart disease and bilateral pyelitis. Spinocaine 2 c.c. Patient died on thirty-fifth day postoperative. Diagnosis, septicemia.

Case 3.—Para ii. Repeat low cervical section. Elective spinal 2 c.c. of spinocaine. Death on eighth day postoperative. Diagnosis, general peritonitis.

Case 4.—Para iii. Chronic nephritis with hypertension. Abdominal hysterotomy and sterilization. Pregnancy three and one-half months. Blood pressure 280/190. Spinocaine 2 c.c. Patient in fair condition at end of operation and remained so until four hours postoperative, when she had a few convulsive movements of face and legs, and died. Diagnosis, cerebral embolus. Autopsy not permitted.

Case 5.—Para i. Decompensated cardiac disease. Hysterectomy of the early pregnant uterus. Spinocaine 2 c.c. Patient died on the third day postoperative of cardiac failure.

Case 6.—Para i. Chronic active pulmonary tuberculosis. Hysterectomy of early pregnant uterus. Patient died seven days postoperative. Diagnosis: pulmonary tuberculosis.

In this mortality group no questionable connection between the anesthetic used and fatal result exists, except in the instance of Case 1. This patient, in my opinion, did not die in respiratory failure or directly from effects of the drug. How much the spinal anesthetic contributed to the existing shock which resulted from the uteroplacental apoplexy and operation, is another question. The fact remains that the choice of anesthesia, my own, in this case was not a judicious one, and serves to illustrate the danger of lumbar anesthesia under these circumstances.

CONCLUSIONS

- 1. Spinal anesthesia has a definite place in abdominal obstetric surgery when the use of general inhalation anesthesia is contraindicated.
- 2. The method is safe only with judicious selection of risks, a careful technic of induction, close observation of the patient during anesthesia, and preparedness for any unfavorable reaction.
- 3. Spinal anesthesia is contraindicated in desperate risks or in conditions in which either shock or hemorrhage is present.

I am deeply grateful to the various obstetricians who have made their private records available to me for this study,

REFERENCES

(1) Kreis, O.: Centralbl. f. Gynäk. 24: 724, 1900. (2) Editorial Am. Surg. 5: 578, 1928. (3) Brindeau, A.: Bull. Acad. de méd., Paris 64: 194, 1926. (4) Delmas: Rev. Franç. de Gynéc. et d'obst. 15: 145, 1920. (5) Krause, H.: Ztschr. f. Geburtsh. u. Gynäk. 86: 598, 1923. (6) Ockerblad, N. F., and Dillon, T. B.: J. A. M. A. 88: 1135, 1927. (7) Sise, L. F.: New Eng. J. Med. 200: 1071, 1929. (8) Pitkin, G. P.: J. Med. Soc. N. J. 24: 425, 1927. (9) Labat, G.: Am. J. Surg. 5: 625, 1928. (10) Ducuring, J.: Bull. Soc. d'obst. et de gynéc. 18: 115, 1929. (11) Phaneuf, L. E.: Surg. Gynec. Obst. 47: 851, 1928. (12) Babcock, W. W.: Am. J. Surg. 5: 571, 1928. (13) De Takats, Quoted from Stout, R. B.: Am. J. Surg. 7: 57, 1929. (14) Labat, G.: Regional Anesthesia Text, ed. 1, Philadelphia, 1924, W. B. Saunders Co., p. 449. (15) Babcock, W. W.: Personal communication. (16) Tendler, M. J.: Memphis M. J. 6: 143, 1929. (17) Brindeau, A., Gagey, J., and Schwaab: Bull. Soc. d'obst. et de gynéc. 18: 31, 1929. (18) Friedman, E.: Monatschr. f. Geburtsh. 75: 163, 1926. (19) Astley, B. G. M.: Am. J. Obst. & Gynec. 13: 83, 1927. (20) Young, J.: Proc. Roy. Soc. of Med. 26: 314, 1929. (21) Johnson, H. W., and Johnson, R. A.: Southern M. J. 23:

390, 1930. (22) Irving, F. C.: Am. J. Obst. & Gynec. 6: 688, 1923. (23) DeLee, J. B.: Surg. Gynec. Obst. 40: 230, 1925. (24) Stander, H. J.: Am. J. Obst. & Gynec. 12: 633, 1926. (25) Joslin, E.: Treatment of Diabetes Mellitus, ed. 4, Philadelphia, 1928, Lea & Febiger, pp. 780, 870, 872. (26) Sise, L. F., and Woodbridge, P. D.: New Eng. J. Med. 201: 506, 1929. (27) Pitkin, G. P.: Am. J. Surg. 5: 537, 1928. (28) Lundy, J. S.: M. J. & Rec. 124: 87, 1926. (29) Sise, L. F.: Current Researches Anesth. & Analg. 6: 163, 1927. (30) Ginginger, A., and Assovatz, S.: Bull. Soc. d'obst. et de gynéc. 18: 267, 1929. (31) Williams, J. W.: Obstetries, ed. 6, New York, 1930, D. Appleton & Co., pp. 641, 644, 997.

19 BAY STATE ROAD.

PRIMARY CHORIOCARCINOMA OF THE FALLOPIAN TUBE, WITH THE REPORT OF A CASE

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THE subject of chorionic tumors is one of great importance, particularly as these growths entail so much danger to the patient. Saenger gave the first clinical picture of the disease in the uterus, Fraenkel and Marchand proved that the cellular elements of the chorionic villus produced the growth. Thus it is fetal in origin and can therefore occur only during pregnancy. Ewing and others have made valuable contributions. After a careful survey of the literature I could find only 19 authentic cases of primary chorionepithelioma or carcinoma of the fallopian tube. The appended case is therefore reported. Hartz makes the statement that 3.5 per cent of all choriocarcinomas occur in the tube. Kelly asserts that this condition following ectopic pregnancy is about as frequent as choriocarcinoma following intrauterine pregnancy.

All embryonic tissue has a potential malignant tendency as shown by its invasion of the tissue at the site of nidation and its dissemination distal thereto. This latter is evident from the presence of chorionic cells in the pulmonary capillaries even in normal pregnancy. The maternal organism, therefore, must possess some inhibitory agency which prevents the extension of this malignant tendency; or what is more probable, there is a difference in the degree of malignancy of the cells constituting the tumor.

The normal villus consists of a connective tissue stroma, covered by two layers of cells, the inner usually a single layer of Langhans' cells, the outer thicker syncytial layer, containing many vacuoles. By an intensive, destructive invasion of the uterine tissue, the villus burrows into and becomes attached to the former. At the line of demarcation a fibrinous reaction takes place, the so-called membrane of Nitabuch. If the invasive process terminates here, normal pregnancy supervenes. If not, one of four conditions may take place: 1. The formation of simple hydatidiform mole, consisting of an active proliferation of the syncytial layer with preservation of the connective tissue core. Mucous

edema gives the characteristic vesicle appearance. There are no new capillaries formed, there is no active destruction of maternal tissue nor tendency to metastasis. This type of growth usually separates and is spontaneously expelled. 2. Choreoadenoma destruens of Ewing, which is similar to the ordinary mole but with greater tendency to deeper invasion and separation of the uterine tissue. However the epithelial cells do not break through the limiting connective tissue barrier nor is there metastasis. 3. Typical malignant form. Both layers of cells undergo malignant changes but either one may predominate. Large cellular masses are seen, marked destruction and vacuolization takes place. The cells show marked mitosis. The chief characteristic is the disappearance

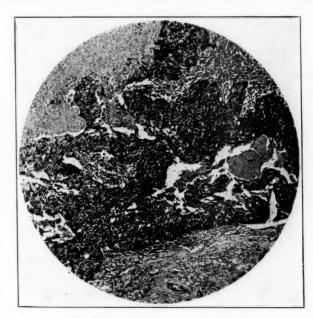


Fig. 1.—Choriocarcinoma. (×100).

of the connective tissue stroma. Metastases take place via the blood vessels. This form is extremely malignant. 4. Malignant syncytioma of Ewing. Instead of both cellular types being represented, the tumor is formed exclusively of syncytial cells. This is much more benign, even metastases undergo retrogression after removal of the primary growth.

It is questionable whether this same classification can be applied to choriocarcinoma as it appears in the tube. However, two recoveries in the series may be traced to the occurrence of the relatively benign form.

The theory has been advanced that hydatidiform degeneration seems to be related to a gradual waning vitality of the germinal cells. This seems contradicted by the fact that the majority of the patients were below thirty-five years of age and one even of seventeen. The author's patient was the oldest of the series, forty-six years. Contrary to the usual history of sterility or one child sterility, as obtains in extrauterine pregnancy, most of the cases of choriocarcinoma of the tube were not only multipara but had a high degree of fecundity, one being a para viii. In the case herewith reported the patient had her last child nineteen years ago.

No case has ever been correctly diagnosed, most of them being mistaken for extrauterine pregnancy, some for ovarian tumors or pyosalpinx. The usual history is that of amenorrhea over a period of six to twelve weeks, severe colicky pains, attacks of syncope followed by irregular uterine bleeding. In a few cases there was a quiescence of symptoms for a few months and in most of them a rather characteristic

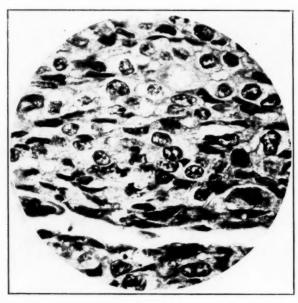


Fig. 2.—Choriocarcinoma. (×700).

progressive asthenia supervened. In the case reported, the patient discharged a decidual cast forty-eight hours after laparotomy. Section confirmed the nature of the tissue, thus proving that nidation and malignant change had not taken place primarily in the uterus. If there is pulmonary involvement, there may be expectoration of blood-tinged mucus or actual hemoptosis. Bowel involvement may occasion hemorrhage and partial or complete obstruction may be produced by pressure from the tumor.

Physical examination, aside from general findings of asthenia with possible beginning signs of cachexia, usually elicits localized tenderness over the site of the tumor, which may or may not be mapped out, depending upon its growth out of the pelvis. Vaginal examination, in a few cases, elicited a secondary growth in the vaginal wall. Recognition

of its nature is of great aid in arriving at a proper diagnosis. Although these occur more frequently by implantation secondary to uterine choriocarcinoma, three cases of tubal choriocarcinoma have shown this vaginal involvement. The uterus may be of normal size, position and consistency or slightly enlarged and softened as is frequent in extrauterine pregnancy. A mass is almost always palpable in either fornix, rather closely applied to the uterus and moderately tender and fixed.

The prognosis is very poor, only two cases in the whole series having recovered. The tumor disseminates either by continuity or through the blood stream. If mostly through the portal system, the liver is involved early; otherwise the lung shows most marked metastases. One case recovered in whom the primary mass only was removed, it being impossible to remove the metastases. It must therefore be remembered that very rarely these secondary deposits may undergo retrogression after removal of the primary growth. Death may be due to cachexia, involvement of lung or liver, copious hemorrhage or intestinal obstruction. Patients rarely live longer than a few months after operation.

The earlier the operative intervention, the better the prognosis and the simpler the operation. If the tumor is still confined to the tube. simple unilateral salpingo-öophorectomy is probably sufficient. If the median half of the tube is the seat of the tumor, it is wiser to do a complete hysterectomy, as the uterine mucosa or wall may be secondarily involved by continuity. If the mass is adherent to the intestine, the presumption should be that it is not a simple adhesion but that the malignant cell has already invaded the intestinal wall. A resection is therefore indicated as extension progresses very rapidly. It is questionable whether liver involvement contraindicates any operative procedure.

A valuable lesson to be learned is the inadvisability of doing a conservative operation on a tube that is the seat of pregnancy. This has lately been advocated especially in cases which at the time of operation have ceased bleeding, the tube being apparently free of all products of conception. This procedure cannot be too strongly condemned. First, the tendency of repetition of ectopic gestation is well known, and second, the incidence of malignancy in embryonal tissue must always be borne in mind. Every tube the seat of pregnancy should be totally removed, preferably with a cornual resection.

The recognition of the nature of the tumor is not difficult, if one is on the lookout for it. It occupies the upper part of the broad ligament, varies in size depending on its age and very early becomes firmly adherent to surrounding structures. Most tumors have a very fine capsule which is the remnant of the thinned out tube. The tumor is usually lobulated and dark red, being very vascular and containing considerable blood clot intermingled with or covering the tumor tissue. The latter is grayish white or yellow and very friable, resembling

placental tissue. The secondary growths show the same lobulated appearance.

Section shows characteristic, large protoplasmic masses, usually vacuolated and containing numerous, deeply staining nuclei. These are the syncytial cells. In other sections are numbers of round cells, containing a single nucleus, representing Langhans' layer. In areas at which the tube wall is not too attenuated, the muscle tissue of the latter may be recognized. Many of the sections show large hemorrhagic areas containing degenerated cells.

CASE REPORT

Patient C. A., white, aged forty-six, married. Her chief complaint was abdominal pain, weakness and vaginal bleeding. The family history was negative as to cancer and tuberculosis. Aside from an operation for varicose veins, complicated by pneumonia, she has always been in good health. Menstruation began at twelve, regular, every twenty-eight days, lasting four or five days, rather profuse. The last few years the periods have been more frequent and of longer duration. She has had two normal pregnancies and labors, the last one nineteen years ago. No miscarriages.

In February 1929, she had a normal period, missed the one of March, but normal again in April, May and June. Since then there has been almost daily bleeding up to date (Nov. 22, 1929). She has suffered moderate lower abdominal pain, remaining localized, since July. Weakness has been experienced during the past three months, without any loss of weight.

Physical examination revealed a rather obese woman, not acutely ill. No abnormal findings or reactions of head or neck. Heart not enlarged, sounds regular, no murmurs, pulse 80 and regular, blood pressure 140/80; vesicular breathing, no râles. The abdomen was large and pendulous, a hard mass made out apparently springing from the pelvis, tender, movable and lying more to the left. Both flanks were dull to percussion. Vaginal examination elicited a firm mass to either side of the uterus, closely adherent to and moving with it. The left leg was swollen and edematous, scars of the old operation being visible. General reflexes were active and equal. The urine, on occasion, showed slight traces of albumin and sugar and many red cells. The tentative diagnosis was fibroid uteri, ascites or malignant ovarian tumor.

Laparotomy was performed under spinal anesthesia, neocaine (0.12). There were very firm intestinal adhesions down to a mass in the pelvis, apparently connected to the left tube, about five inches in diameter, irregular, filled with blood clots and placental-like tissue. The uterus was enlarged, about four inches in diameter and distinctly softened. The right tube was slightly thickened and the fimbria closed. The right ovary contained a small cyst. In places there was a suggestion of a capsule surrounding the mass. The adhesions were separated with considerable difficulty, the tumor mass delivered and removed. Right salpingo-oöphorectomy was performed, leaving a stump of the right ovary. The abdomen was closed in layers without drainage.

The first day postoperative the patient coughed considerably, due to a small area of consolidation at the right base, which cleared up within a week. On the second day she discharged some tissue from the vagina which seemed to be a decidual cast. Vaginal bleeding ceased on the sixth day. She left the hospital on the fourteenth day, wound healed by primary union, moderate induration in

the left fornix. X-ray examination of the chest at this time failed to reveal the presence of any metastasis.

Pathologic report: Specimen consisted of a mass measuring about $10 \times 7 \times 5$ c.m., made up of ovary, tube and broad ligament. On section it appeared at places hemorrhagic, at places granular. This latter was yellow, friable and looked grossly malignant. Section showed extensive tumor necrosis, in general appeared like decidual tissue, containing numerous giant cells, The picture is that of a highly malignant tumor, choriocarcinoma.

Section of tissue expelled from vagina is that of normal decidua, no evidence of malignancy or hydatidiform mole.

The patient did quite well for two weeks after leaving the hospital. Then she began to complain of generalized abdominal pain, weakness, and occasional cough. There had been no vaginal bleeding since the eighth day postoperative. The hard induration in the left fornix was still present and the fundus uteri much smaller. Three weeks later there was occasional bloody expectoration, a tender mass was palpable in left umbilical region, no vaginal changes noted. She was referred to the General Memorial Hospital for radiation, died suddenly the following day, about seven weeks postoperative.

The autopsy showed: "Metastases to the liver and abdominal nodes, partial intestinal obstruction from pressure of tumor, extensive hemoperitoneum (hemorrhage from recurrent tumor mass, the immediate cause of death), decidual reaction in uterus. Sectional congestion of bronchi but no tumor of lung."

REFERENCES

(1) Cope and Kettle: Proc. Roy. Soc. Med. 6: 247-259. (2) Rossier: Gynec. Helvetica 13: 67. (3) Jeanneret: Rev. med de la Suisse Normande 33: 337. (4) Hugier and Louvain: Bull. et mém. de la Soc. Anat. de Paris. (5) Hartz: Surg. Gynec. & Obst. 23: 602, 1916. (6) Lofquist: Zentralbl. f. Gynec., No. 30, 1909. (7) Phillips, J.: J. Obst. & Gynec. Brit. Emp. 19: 502, 1911. (8) Nagelsbach: München. med. Wehnschr., No. 4, 510. (9) Bazy: Ann. de Gynec. & d'obst., April, 1913. (10) Cottalorda: Gynec. et Obst. 4: 119, 1921. (11) Jellett: Trans. Roy. Acad. Med. Ireland 31: 357. (12) Teacher: J. Obst. & Gynec. Brit. Emp. 4: 1903. (13) Risel: Ztschr. f. Geburtsh. u. Gynäk. pt. 56, p. 154. (14) Sunde: Acta obst. et gynec. Scandinav. No. 1, 1920. (15) Gebhard, C.: Ztschr. f. Geburtsh. u. Gynäk. 37: 504, 1897. (16) Hinz, G.: Ztschr. f. Geburtsh. u. Gynäk. Berl. 1: 419, 1895. (18) Nikiforoff, T. N.: Russich. Arch. f. Path. 1: 257, 1896. (19) Senarclems: V. de These de Lausanne, 1902. (20) Snegirew, W.: Mayotschuja Krowotelschenija Moskau, ed. 2, p. 197, 1895. (21) Thorn: München. med. Wehnschr. 44: 1400, 1897. (22) Vassmer, W.: Path.-Anat. Arb. Joh. Orth. Z-Prof. Jubilaum Berl. pp. 237-77, 1903. (23) Vieting, Ernst: Inaugural Dissertation, Univ. Wursburg, 1910. (24) Solomons, B., and Smith, E. C.: J. Obst. & Gynec. Brit. Emp. 30: 162-171, 1923. (25) Strong, L. W.: Proc. N. Y. Path. Soc. 19: 71, 1919. (26) Schmitz, H., and Hueper, W.: J. A. M. A. 95: 1413, 1930.

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REPORT OF A DOUBLE MONSTER, ISCHIOPAGUS*

BY SAMUEL LUBIN, M.D., BROOKLYN, N. Y.

Patient, E. S., thirty-five years of age, an American Jewess, was admitted to the Prospect Heights Hospital on the nineteenth of August, 1930, in active labor. She had been married eight years, had always enjoyed good health and had never undergone any surgical operations, although she had uterine fibroids, discovered during routine pelvic examination several years before, and had never received treatment of any kind including irradiation.

Her menstrual history was essentially negative, her last menstrual period November 24, 1929.

There were two previous pregnancies, one having terminated in a spontaneous two months' miscarriage over six years previously. The second pregnancy resulted in a full-term living female baby, weighing 7 pounds, delivered by forceps because of a prolonged labor, five years ago. This child was born with a ptosis of the left lid and an internal strabismus of the left eye which still persists, although the youngster enjoys very good health and mentality.

The present pregnancy was uneventful. The membranes ruptured spontaneously at 11:00 P.M. on the eighteenth of August, 1930, followed by the onset of labor at 11:30 P.M. The pains began coming rather frequently almost from the onset, and at 12:00 o'clock were about two minutes apart, very painful, and with considerable pressure on the rectum. The patient was admitted to the hospital at 12:30 A.M. on the nineteenth of August, 1930, with pains every minute, and the head on the pelvic floor. The abdomen seemed to be rather large, considering that the membranes had ruptured one and a half hours before. One fetal heart was heard in the left lower quadrant with a rate of 144 per minute. The position could not be determined abdominally. Vaginally, the head was on the pelvic floor with the sagittal suture in the right oblique diameter, and the small fontanelle at the left iliopectineal eminence. Because of the rapidity of progress and the severe pain associated with the uterine contractions, ether was administered with each pain when the perineal stage was started. In spite of the strong uterine contractions, the head seemed to advance slowly and finally delivered itself spontaneously at 1:30 A.M., followed by the shoulders. Following this, difficulty was encountered; the hips would not deliver. By passing the fingers along the hips, a very marked widening of the fetal breech was felt which suggested the possibility of a monster. By sweeping the fingers around to the back of the fetus which was on the left, a hard protruding member was felt which was delivered under the symphysis by bending to the right. This was followed by one pair of legs which were helped over the perineum with moderate difficulty, and was continuous with an after-coming trunk. With considerable effort the shoulders were delivered, the anterior shoulder first. Then the after-coming head would not budge with traction from below or pressure from above; therefore forceps were applied. As the handles were being locked, a gush of clear liquid resulted which later proved to be from the crushing of a hydrocephalic head. A right mediolateral episiotomy was performed and the head delivered with moderate traction on the forceps below and pressure from above. During the latter part of the procedure ether anesthesia was given to the surgical degree. Although the fetus was stillborn, it is possible that the first baby made several respiratory move-

^{*}Presented before the Brooklyn Gynecological Society, April 3, 1931.

The placenta was expressed after the signs of separation appeared at 1:50 A.M., and seemed to be perfectly normal, and 1 c.c. of pituitrin was given hypodermatically. The episiotomy was repaired immediately, using No. 2 chromic catgut. There were no gross cervical lacerations and no tendency toward an atonic uterus.

There was an uneventful recovery, the patient getting out of bed on the tenth day and going home on the thirteenth day. During her stay in the hospital all laboratory findings were essentially negative, including the blood Wassermann test.

The patient presented herself at the office for postpartum examination six weeks following her discharge from the hospital. In the meantime there were two menstrual periods, the first starting on the twenty-second of September, lasting five days, and the second starting on the sixth of October, also lasting five days. Pelvic examination showed a well healed perineum; a cervix in the axis of the vagina and essentially negative; the fundus was in the midline, firm, freely movable, about the size of a six weeks' gestation, and studded with pea- to marble-sized fibroids; the fornices presented no gross pathology.



Fig. 1

A study of the specimen revealed the following: A double monster joined at the pelvis (ischiopagus), consisting of two heads, two pairs of arms, two trunks and one set of male genital organs, set upon one pair of well formed lower extremities. With the trunks in a straight line, the monster measured 22½ inches from the top of the heads. The total weight was 8½ pounds (minus the fluid which escaped from the crushed hydrocephalic head of baby No. 2). The head of baby No. 1 was well formed and anatomically correct, while that of baby No. 2 was a hydrocephalic associated with a double harelip, cleft palate, and a rudimentary right eye which was represented by a folded slit.

There existed an eventration through an opening about two inches in diameter, in their common abdominal wall, with an exposure of the small intestine and what apparently was liver; the umbilical cord entered through the left inferior border of this opening.

The arms of both parts were well formed as also were the one pair of common lower extremities and the male genital organs, which were normally situated with the anal opening behind.

Coming off for a length of five inches from the joining of both spinal columns posteriorly was a skin-covered bony structure which tapered from the base, which was about one inch in diameter, to the end, which was about one-quarter inch in diameter, and had a joint one-third inch from the tip. This apparently was a rudimentary lower extremity and will be described further in the x-ray report.

On autopsy by Dr. L. Albert Thunig the following was noted:

Baby No. 1. A normal sized thymus gland. The lungs were normally developed and showed evidence of having functioned. The diaphragm was completely formed, separating the abdominal from the thoracic cavities. The heart showed a patent foramen ovale in a very thin-walled interauricular septum. The ductus arteriosus was closed. The heart valves were well formed.

Baby No. 2. Thymus was quite small, but larger than the size of the heart. The lungs were contracted, small, and the surface was granular. The right lung showed an ill-defined middle lobe, and the left a poorly defined cleavage between the upper and the lower. On section they were solid and contained a frothy serum showing evidence of this baby having breathed. The diaphragm was completely

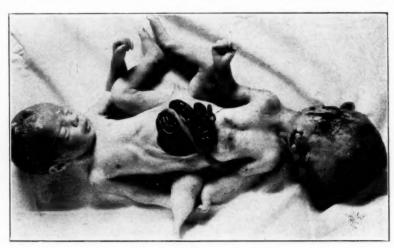


Fig. 2

intact, separating the abdominal from the thoracic cavities. The heart appeared to be embryonic, being only three-quarters inch long, one-quarter inch thick, and one-half inch wide with a typical cone-shaped embryonic left ventricle. The right ventricle was a small mass about one-quarter inch in size on the anterior surface of the heart and had no openings into its cavity, and was purely rudimentary. There was complete absence of the right auricle. There was no valve formation, between the left auricle and ventricle, but there were two pulmonary veins emptying into the left auricle which was only rudimentary. The vena cava emptied into the junction of the rudimentary pulmonary artery and the arch of the aorta. The heart of this baby was merely a tubular organ which served no function other than that of a blood vessel, through which the blood passed, and the circulation was maintained by the heart of baby No. 1.

The common abdominal wall presented an opening about two inches in diameter, through which there was an eviseceration of small intestine and part of the liver from each fetus. There was one small intestine in each fetus which joined in the ileum to form a double ceeum which passed upward into a single ascending colon. Each segment of the bifurcated eeeum had its own appendix attached.

The spleen, stomach and pancreas appeared grossly normal on both sides. The liver of baby No. 2 is about one-quarter the size of that of baby No. 1.

There was one large fused kidney with one ureter coming from a single pelvis situated centrally on the ventral surface. The bladder was normally situated, was thick and hard, and contained one-half ounce of urine when opened. The urethral orifice was visible, but could not be probed, probably due to formalin hardening. There was another large kidney on the right side of baby No. 2 which was anterior and closely adherent to the liver, was markedly cystic at the lower pole, and had one ureter which emptied into the bladder.

From the autopsy findings it seemed as though baby No. 1 was almost a normally developed baby, and furnished the heart action for both babies. Baby No. 2 showed a great many abnormalities and was dependent on baby No. 1 for its blood supply. Even though from outward appearances this monster appeared symmetrical, each section equally developed, yet the autopsy findings would suggest a parasitic tendency from the standpoint of circulation on the part of baby No. 2 to its host. The circulation of both babies was joined at the pelvic brim which harbored a common iliac artery and an accompanying vein which was continuous with the abdominal aorta and the inferior vena cava, respectively, in each fetus.

The blood coming from the placenta through the umbilical vein in the major portion made its way to the heart of baby No. 1, whence it was propelled to the tissues of the entire monster and also back through the umbilical arteries to the placenta.

The placenta presented no gross abnormalities. There were no infarcts, accessory lobes, cysts, extravasation of blood, calcareous degeneration, or other conditions which might tend to attribute the cause of the monstrosity to some systemic condition in the mother, or to a local condition in the placenta.

Roentgenologic examination by Dr. Frederic E. Elliott showed two fairly normal fetal skulls; two complete spinal columns with normal development of the upper shoulder girdle and upper extremities. The pelvic girdle of each fetus was lost in a confused conglomerate, purposeless bone formation. The lumbar spines of each fetus entered into this mass from the opposite axes of the spines. On one side were the normal bony structures of the lower extremities without, of course, normal articulation to the pelvic girdle, and between these extremities could be seen the soft parts of a male fetus. On the opposite side was a single extremity with a well-developed fetal femur and rudimentary bone development of the tibia was seen. In other words, there is the image of a monster, the heads, upper extremities and bodies of each appearing fairly normal, with a disorderly fusion of the pelvic girdles, from one side of which was a well-developed, normal set of bones for the lower extremities and on the other side a rudimentary single thigh and leg formation.

The author wishes to express his appreciation to Dr. L. Albert Thunig and Dr. Frederic E. Elliott for their great cooperation in the pathological and roent-genological examinations.

777 PROSPECT PLACE.

REPORT OF A CASE OF ABNORMAL FETUS FOLLOWING RADIATION OF THE MOTHER

BY IRA I. KAPLAN, B.S., M.D., NEW YORK, N. Y.

(Director Division of Cancer, Department of Hospitals, and Radiation Therapist, Bellevue Hospital)

THE effect of radiation on the oncoming progeny remains a much mooted question. Various suppositions have been offered as explanations for the birth of abnormal children of radiated mothers. Abnormal children have been born following the radiation of the mother, but then, too, radiated mothers have given birth to normal offspring as reported by Williamson, Rubin, Kane and myself.

It is axiomatic in radiation therapy that the more embryonic the tissue the more sensitive it is to the effect of the x-rays. A fetus, being obviously most embryonic in character, should therefore be extremely sensitive to x-rays. The age of the fetus has a great deal to do with the degree of sensitiveness as is evident from the report of the births of a number of children following radiation applied to them in utero. Moreover, examination of several fetuses removed from the uterus following irradiation of the mother showed the embryo unharmed by the rays. It is no doubt reasonable, however, to assume that a very early fetus formation in utero is definitely destroyed by the x-rays. Parkes claims that the termination of pregnancy is the most striking result at that period. This has been shown in such cases where the x-rays had been used to abort a pregnant mother, as reported by Wyser and others. In the treatment of amenorrhea and sterility the x-rays have been used as a stimulating agency and children born following such treatment of the mother had been normal and healthy. For this reason the birth of the abnormal child in the case herewith reported is of especial interest.

L. M., married, aged twenty-seven, has one child four years old. Since age of eighteen had been under treatment by a competent gynecologist for irregular menstruation, miscarriage, and sterility. She miscarried in March, 1929, menstruated in May, 1929, and September, 1929, her last menstruation occurring in November, 1929, and none appearing up to April, 1930. Radiation was suggested in that month. Before receiving x-ray treatment she was examined by her gynecologist and the presence of gestation in the uterus was not noted. The patient herself stated she was not pregnant. Accordingly x-ray therapy was given on April 9, 15, and 22, a total dose of 12 per cent being delivered to the ovaries. A month later the patient reported that evidently no action had followed the x-ray treatment. In June she reported being pregnant, went into labor November 1, and was delivered of a stillborn child which was abnormal in form. Described by the attending physician as follows: Stillborn monstrosity, hydrocephalic, distorted atrophic features, rudimentary nares, body fairly well developed, extreme polyhydramnios present.

The question arises as to the cause of the malformation of the fetus. Was it a postradiation pregnancy? Was the patient already pregnant at the time of radiation and did the x-rays adversely affect the fetus in utero? Why did not the irradiation of the patient abort the damaged embryo? Why did not the embryo fail to develop if it were damaged at its inception? Why did the patient and the gynecologist fail to note the pregnancy earlier?

We can only offer suppositions in reply, since no definite knowledge is as yet available as to the reason for monstrous formation of the fetus in women who have never had radiation. The statistics from DeLee, Case and Cooper, and Hirst indicate that monsters are a frequent occurrence in the ordinary run of obstetric cases.

Did pregnancy in this case occur in a damaged ovum? In our experience we have had many examples of healthy normal children being born of mothers who became pregnant shortly following the administration of the same type of x-ray therapy as given to this patient, as reported by Rubin, Rongy, Schmitt, Bollaffio, Doderlein and myself. But the possibility of a damaged ovum becoming fertilized cannot, however, be ruled out. Since, as already stated the more embryonic the tissue the more radiosensitive it is, we may suppose that this patient may have become pregnant at the time of irradiation and the newly-formed embryo was so sensitive to irradiation as to be definitely damaged thereby. On the other hand, if the embryo is so sensitive to irradiation, then according to workers who have studied the abortive effects of x-rays, this fetus should have been extruded dead following treatment.

From this patient's clinical history, and sterility, it would appear that the embryo in all probability would not in any case have developed normally. Whitehouse says that any change in the environment will alter the development of the normal fetus. One of the established causes for the birth of monstrosities is the change of environment in the birth canal due to the long period of sterility before conception. Mall states that the faulty implantation of the ovum causes an imperfect formation of the fetal coverings and that this faulty implantation is due to some condition of the uterus and the result may produce monstrosities. According to the general causes of teratogenesis, any abnormal disturbing force may interfere with the proper developmental growth of the embryo.

⁵⁵ EAST 86TH STREET.

REPORT OF A CASE OF HYPEREMESIS GRAVIDARUM WITH NECROPSY

By M. T. HARRISON, M.D., ATLANTA, GA.

ON DECEMBER 5, 1930 I was called to see a colored woman aged twenty-six, who previous to her marriage two years before was a graduate nurse. Her appendix was removed in 1924; tonsils in 1927; and on July 4, 1930 when six weeks pregnant, an abortion was induced because of uncontrollable vomiting.

Following the abortion on July 4 she menstruated once. She missed her monthly period expected early in September and during the last week in September became nauseated. She called her family physician who diagnosed the condition as the nausea of pregnancy. She did not respond to his treatment and on November 19 was transferred to an Atlanta hospital.



Fig. 1



Fig. 2

Fig. 1.—Heart, showing cloudy swelling of fibers, fragmentation, nuclei obscurity, and edema. (High power.)

Fig. 2.—Kidney, showing marked degenerative changes in the tubules. The normal histologic cells are degenerated. Only the structural tissues remain. There is also some cloudy swelling. (High power.)

She was placed on limited fluid intake, alkalies, and a carminative prescription by mouth. Glucose 2 per cent in normal saline was administered daily by rectum. Her room was quiet, visitors were restricted and she was given mild sedatives with an occasional small dose of morphine and scopolamine. The first week she vomited almost every liquid taken by mouth. On the twenty-sixth she vomited very little and apparently enjoyed what nourishment she was given. Until December 4 there seemed to be slight daily improvement. On the morning of this day the nurse detected a rapid pulse and made the following notation on the chart "patient acts queerly at times." Her physician was notified. He ordered 1 c.c. of digifoline every four hours and four grains of calomel. Normal saline was given under the skin and by rectum.

Her temperature had ranged from 97° to 99.8° F. with an average close to normal. Her pulse had varied from 88 to 122 with an average between 90 and 100.

The most notable observation was obstinate constipation. In fact not one entirely satisfactory bowel movement was recorded.

Examination on December 5 at 1:30 A.M. disclosed an emaciated colored woman who answered questions rather slowly and who seemed more or less dazed. The skin was dry and the feet cold. Her blood pressure was 100/88; temperature 97.8°; pulse 140 and respirations 26. The lips were dry and fissured. There was no glandular enlargement in the neck. The lungs were clear and other than a rapid rate the heart appeared normal. The abdomen was distended. The percussion note was tympanitic. Above the symphysis could be felt the upper border of an oval mass. The cervix was soft and deep in the pelvis. The uterus was outlined above the cervix and was approximately 15 cm. in diameter.

The clinical diagnosis was hyperemesis gravidarum, with a very discouraging

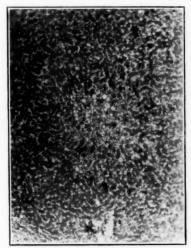


Fig.

Fig. 4

Fig. 3.—Liver, showing areas of marked fatty degeneration and infiltration. (Low power.) (These areas are numerous throughout organ.)
Fig. 4.—Liver, showing fatty change. (High power.)

outlook. Intensive supportive measures were instituted. For about twelve hours there was some improvement after which she began to decline and died about twenty-four hours later. Three hours after death a necropsy was performed by Dr. J. C. Norris whose report follows:

The heart was not enlarged. The right side was soft and dilated. The liver was normal in size but was pale and flabby. The cut surface had a greasy appearance. The spleen was soft and was slightly enlarged. The kidneys were swollen and showed cortical petechiae. There was a moderate nephritis. The uterus was soft, 16 cm. in diameter and contained a four months' fetus. The placenta overlies the internal os.

The anatomic diagnoses were: (1) Generalized toxemia: (a) Toxic myocarditis with dilatation, (b) congestive pneumonitis, (c) toxic hepatitis, (d) toxic splenitis, (e) toxic nephritis. (2) Dehydration, (3) anemia, (4) pregnancy at four months with placenta previa.

Blood chemistry: Sugar 60 mg. per 100 c.c. Nonprotein nitrogen 100 mg. per 100 c.c. The histologic diagnoses are: Congestion of pulmonary alveoli, edema; cloudy swelling of heart cells; fatty degeneration and infiltration of liver, with cloudy swelling; cloudy swelling and hyperplasia of spleen; cloudy swelling with degenerative changes of kidneys, marked in the tubules. The glomeruli are hypertrophied. The vessels are empty.

1111 MEDICAL ARTS BUILDING.

A COMPARATIVE STUDY OF MERCUROCHROME AND HEXYLRESORCINOL AS ANTISEPTICS DURING LABOR*

BY HAROLD B. HENDERSON, M.D., DENVER, COLO.

(From the Department of Obstetrics and Gynecology, University of Colorado School of Medicine and Hospitals)

THIS study is an extension of a previous report of "Mercurochrome as an Antiseptic During Labor," published in *Colorado Medicine*, June, 1930. At that time 200 cases were reported: 100 in which mercurochrome was used as an antiseptic during labor, and 100 cases of controls in order to obtain the comparative percentage of lowered morbidity and possibly mortality.

To this series are now added 300 more cases: 100 each in which mercurochrome and hexylresorcinol respectively, were used as antiseptics during labor, and 100 more control cases.

The standard of morbidity varies in the different clinics, and the percentage varies accordingly. Any patient whose temperature reaches 100.4° F. on two successive days following delivery, not including the day of delivery, and occurring not later than the tenth day, we have considered a "morbidity." This is the standard accepted by the Johns Hopkins Hospital. This is practically the same standard as that of the American College of Surgeons. The University of Michigan considers as morbid all eases showing a temperature of 100.4° F. at any time from delivery to discharge, temperatures being taken every four hours. Goodall and Wiseman prefer to consider as morbid all eases in which the temperature exceeds 99° F. on any three consecutive days, exclusive of the first twenty-four hours; and in addition, all cases that are morbid but afebrile, such as subinvolutions and thrombophlebitis.

Mayes reports results with the employment of mercurochrome in over 10,000 consecutive cases which showed a lessened morbidity of more than 50 per cent. He also claims that it is a valuable procedure before cesarean section, induction of labor, and vaginal examinations.

Our technic was that of Mayes without quite as an extensive spraying of the thighs. The maternal morbidity of 200 consecutive cases in which mercurochrome was not used was 52.25 per cent higher than the maternal morbidity in 200 consecutive cases in which mercurochrome was used, and 37.50 per cent higher than in the series of 100 cases in which hexylresoreinol was used as an antiseptic during labor.

The hexylresorcinol was used in this small comparative series because of both its colorless and nonirritating nature, and although the results are not definitely conclusive, they compare very favorably with the larger mercurochrome series.

^{*}I am indebted to Dr. W. H. Mast, Resident Physician at the Colorado General Hospital where this series was observed, for his help in reviewing these cases.

In view of the fact that our figures fairly well corroborate those of Mayes in respect to mercurochrome and our own observations with hexylresorcinol, we desire to report them with some little enthusiasm, and because of a certain added sense of security which the procedure of the use of antiseptics during labor gives to the mind of the obstetrician, especially in those more critical and difficult situations.

509 REPUBLIC BUILDING.

REPORT OF TWO CASES OF RUPTURED LIVER IN THE NEWBORN

BY H. J. RUSSELL McNitt, B.S., M.D., WASHINGTON, D. C.

RUPTURE of the liver in the newborn seldom has been described in literature. The usual history of the case is found in an apparently normal child, who within three or four days of birth, suddenly becomes ill and dies rapidly within a few hours.

Hepatic injury is the most common of intraabdominal traumatisms, but actual rupture of the liver is the least common of all the various forms of injury. Death in actual rupture is postponed as a rule for three or four days, during which time a subcapsular hemorrhage is slowly taking form. When the pressure of the blood within reaches the proper proportions, a rapidly fatal intraabdominal hemorrhage results.

The usual cause of this condition is pressure or torsion of the fetal abdomen. Usually there is a history of definite external trauma to be found, although there has been reported a case in which the birth was spontaneous, rapid, and not attended by any external manipulation before birth or immediately afterward.

CASE 1.—Mrs. E. M., aged twenty-nine years, married. Three full-term labors with two forceps deliveries.

History of present pregnancy: The last menstrual period was on March 10, 1930. The prenatal physical examination was essentially negative, except for some dental caries. Her measurements were normal and the coccyx was movable. The patient's height was 61% inches, and she weighed 110 pounds.

The blood pressure during her prenatal period varied from 96/60 to 120/80. At no period did she have any edema of the feet or bleeding from the vagina. Toxic symptoms were never present, and except for an occasional attack of constipation, her bowels were always free. Active fetal movements were felt during the fourth month.

On the sixteenth of December, one day before the estimated date of confinement, the patient went into labor. At this time the position was R. O. P., and the fetal heart strong. After six hours of hard labor with the cervix practically dilated, the position was still R. O. P. The abdomen was manipulated between pains with the end in view of turning the fetus, this was accomplished quite easily, and about twenty minutes later a baby boy, weighing 8 pounds was born.

The child took the breast well and appeared perfectly normal. Two days later, the baby suddenly vomited, its respiration became more rapid, and its skin very anemic in appearance. One hour later it died. Artificial respiration failed, as did intracardiac injections of adrenalin.

The autopsy findings were as follows: On opening the abdomen, many large clots of blood were seen. These were readily washed out with running water, but on examining the upper abdomen, a large clot was seen to be more firmly attached to the under surface of the liver. On close examination, a rent in Glissons capsule, approximately one inch in length was found, and beneath this, a corresponding laceration of the liver substance. This tear extended from a point on the inferior surface of the right lobe near the vertebrae, laterally, and forward for the distance of one inch. A clot was firmly attached to the bed of the laceration. All organs were anemic in appearance. The tentorium cerebelli showed no laceration or hemorrhage.

Case 2.—Mrs. D. P., aged twenty-three years, white. Previous pregnancies: twins, died when three days old, cause unknown, no autopsy. Last menstrual period, January 19, 1930. Quickening at four and one-half months. During the eighth month there was some slight bleeding with no pain. Subsided after one week in bed. No return. Urine negative. On October 31, 1930, the patient went into labor at 4:30 A.M., the membranes ruptured at 4:00 A.M. and birth of a male infant weighing 9 pounds 3 ounces took place at 7:35 P.M. on the same day. The position was L.O.A. Ether anesthesia was used and there was a loop of cord around the infant's neck. Three days later, on the third of November at 4:30 P.M. the baby apparently became very hungry (thirsty?), regurgitated, grew pale, defied all attempts at resuscitation, and died at 12:30 A.M. The child's temperature ranged from 99° to 101.8°.

At the end of the second stage of labor, mild pressure was exerted on the abdomen during pains in order to assist the slow descent of the large child through the birth canal. This was the only antepartum manipulation made.

Autopsy Report: Intraabdominal hemorrhage of dark thick blood. A large clot was found toward the posterior inferior aspect of the right lobe beneath the capsule of Glisson, filling the proximal portion of the right lateral gutter. Dissecting up the capsule of Glisson, almost over the entire postinferior aspect of the right lobe, the subcapsular hemorrhage measured $2\frac{1}{2}$ inches by $1\frac{1}{2}$ inches. On removal of the liver, a more or less eliptical slit or rupture was noted in the capsule extending toward the lateral aspect of liver margin.

I present these two cases merely to show the possible sequelae of antepartum manipulations, even though they may be of quite gentle nature. I feel that a certain percentage of deaths occurring in this period of three to four days following delivery would fall in this group of liver injuries if more autopsies were done on these babies.

I am indebted to Dr. Chester Brady, of this city, for the second case report. 1835 Eye Street, N. W.

REPORT OF A CASE OF ACUTE APPENDICITIS COMPLICATING LABOR WITH PREECLAMPTIC TOXEMIA

BY BEN-HENRY ROSE, M.D., NEW YORK CITY

D. E., aged nineteen, female, white, married. Last period March 22, 1929; date of expected labor, December 27, 1929.

Patient came to see me at 9 A.M. on December 11, 1929, with the history that she was awakened with a severe attack of pain in the right upper quadrant about 4 A.M., with vomiting of bile, pain persisting without relief. She had had a natural bowel movement. She had not been to see her physician for the past three months. In fact, she worked as a salesgirl in a department store until the day previous, wearing a tight corset!

The patient had blood pressure of 158/100, and examination showed a full-term gravidity. There was some tenderness over the region of the gall bladder, none on palpation over the other quadrants of the abdomen, some tenderness of percussion over the costovertebral angle. Both legs were edematous. Rectal examination did not reveal any cervical dilatation. Urine showed albumin (++++), granular and hyaline casts, some blood but no pus cells. A diagnosis of preeclamptic toxemia was made and the patient was advised as to the diet and hygiene. She returned at 7 P.M. on the same day, not having had any opportunity to follow the prescribed instructions, complaining of severe and agonizing persistent pain in the right lower quadrant of the abdomen. She had vomited several times during the day. The pain was so severe and agonizing that she could not sit quietly for even a few minutes. Physical examination revealed marked tenderness on palpation over the right lower quadrant of the abdomen with definite rebound tenderness present. Pain was increased on elevation of the thigh on the abdomen. There was spasm of the right rectus muscle. There was tenderness on percussion over the right costovertebral angle. Rectal examination revealed that the cervical os was 3 fingers dilated. The rectal temperature was 99.8°, pulse 90, respirations 20. Blood count: Total white blood cells 15,800. Polymorphonuclear leucocytes 82 per cent, basophiles 1 per cent, lymphocytes 17 per cent.

The patient was seen again three hours later. The pain still persisting in the right lower quadrant without radiation, and the rectal examination revealing a cervical dilatation of 4½ fingers, she was sent to the hospital. As the patient was being prepared, the membranes ruptured and caput appeared. Because of the persistence and localization of the pain to the right lower quadrant, because of the blood count and the absence of pus cells, a diagnosis of acute appendicitis complicating labor was made, and it was decided to open the abdomen directly after the fetus was born; under gas oxygen analgesia, a living male fetus was delivered. The afterbirth was delivered, no pituitrin or ergot was given, and the anesthesia continued.

Operation: McBurney intermuscular incision, peritoneum opened, free sero-sanguineous fluid escaped, a large markedly congested appendix, covered with some plastic exudate, distended at the tip, was found and removed between clamps. The stump was ligated, phenolized and alcoholized, and tied to the stump of the meso-appendix. The abdomen was closed in layers, no drainage.

The patient made an uneventful recovery; the lochia was normal; and there was no marked postoperative distress aside from that which normally follows an appendectomy. The wound was healed by primary union, and the mother and child were discharged on the eighteenth day.

REFERENCES

Anderson, A. W.: Nebraska M. J. 8: 102, 1923. Cocke, N. P., and Mason, J. M.: J. A. M. A. 75: 95, 1920. Davis, E. P.: Complications of Pregnancy, Obst. and Gynec. Monogr., p. 154, 1923. Idem: Progrès. méd. 3: 34, 1924. DeLee, J. B.: Personal communication. Idem: Surg. Clin. N. Am. 1: 100, 1921. Idem: Principles and Practice of Obstetrics, 1928, p. 527. Ehrenfest, H.: Personal communication. Faverau, M., and Chaput, L.: Progrès méd. 38: 133, 1923. Fincklen, E. A.: New Orleans M. & S. J. 78: 146, 1925. Findley, P. J.: J. A. M. A. 59: 612, 1912. Grattan, J. F.: Surg. Gynec. Obst. 29: 457, 1919. Heineck, A. P.: West Virginia M. J. 12: 127, 1917. Idem: 12: 292, 1919. Idem: M. Herald 46: 340, 1927; 47: 4, 1928. Hirst, B. C.: A Textbook of Obstetrics, 1924. Portes and Seguy: Gynecologie and Obstetrique 15: 114, 1927. Royston and Fisher: Am. J. Obst. & Gynec. 11: 184, 247, 1926. Wallace, C. J.: J. A. M. A. 64: 737, 1915. Williams, J. W.: Personal communication. Idem: Obstetrics, p. 571. Wilson, R. A.: Surg. Gynec. Obst. 45: 620, 1927.

229 EAST KINGSBRIDGE ROAD.

CHINESE CUSTOMS AND TRADITIONS OF CHILDBIRTH WITH BIRTH STATISTICS FOR SAN FRANCISCO*

BY JOSEPH SHIANG-MIN LEE, † M.D., SAN FRANCISCO, CALIF.

THIS paper records some of the customs and folklore of Chinese women in pregnancy and labor, few of which longer obtain among the Chinese resident in San Francisco. In fact, hardly any of them are accurately known to the younger women here, who are mostly now of the third or second generation of Chinese women born in San Francisco.

The old traditions gradually fell into disuse for a number of reasons. Contact with Americans, observations of their customs and laws, the influence of the public schools, the immigration laws and the recognized need for proper registration of births and deaths have changed the conditions. The first generations here utilized the older women relatives as midwives; those who came later employed women physicians. At the present time, no licensed Chinese midwife is practicing among the Chinese in San Francisco. Last year every birth in the Chinese quarters was reported by physicians. Even to the older generation, the customs of older China here described remain but a hazy memory.

In fact, it was not easy to obtain the data for this paper. The male Chinese physicians have never had obstetric practice. In older times they were never called into consultation by the amateur midwives except in case of desperate emergency. Often they were sought only for medicine. This older generation has passed away. This data were obtained from such old women as had in the past officiated as midwives during the confinement of their daughters-in-law, relatives and

^{*}Contributed to the White House Conference, as a part of the report of the Subcommittee on Factors and Causes of Fetal, Early Infant, and Maternal Morbidity and Mortality—Hugo Ehrenfest, M.D., Chairman. †Assistant in Medicine, University of California Medical School.

friends as in old China. There each locality had its own practices and customs, considerably modified by the religious and ancestor-worship customs of each individual community.

There is evidence to believe that Chinese women rarely have serious difficulty in labor. Childbirth with them is relatively easy. The lying-in period is very short. Their labors support the view that women who live simpler lives have easier labors than their more luxurious living sisters and that women from villages and small towns are less likely to have dystocia than those who live in the cities.

The older generations had comparatively few rules to guide the pregnant woman. She continued to do her housework or other daily occupation. She was advised to be moderately active up to the day of labor.

There was comparatively little restriction of diet: only a few generally recognized principles of eating. Crabs and shrimps were not eaten because it was known that they might cause urticaria. Lamb and mutton were avoided since it was thought that they might cause the child to have epilepsy. Whether there is or is not basis for this belief may not be known, yet the word "YEUNG" meaning lamb is compounded in the Chinese expression for epileptic fits. On the whole, a diet of easily digested simply cooked foods was taken.

The mother-in-law or midwife was called into attendance at the time of childbirth. There was no preparation for the labor; very little was done to prepare the mother. Nature was allowed to take its course; patient waiting was the rule. The child was allowed to be born without assistance, if possible. No examination was made to determine the presenting part either during pregnancy or labor. Any deviation from the normal labor was ascribed to some disease of the mother, some condition of her blood, poor health, bad temper, or the machinations or bad influence of the devil.

When the patient came into definite labor, she assumed a squatting position, either on the bed or on a low stool. This seems most natural since it calls to the patient's aid the help of the force of gravity. During the minutes of severe pains, the midwife and friends gave such physical assistance as they could offer by pulling against her arms, and talked to her attempting to encourage her. Medicines were used if there was any difficulty in delivery. They were mainly concoctions of herbs, taken by mouth to stimulate the muscles and abolish fatigue. But if the medicines did not help her, there was little hope either for the mother or the child. On the rare occasions of malpositions, the more brave midwife might attempt version, done without any scientific knowledge. Yet, if these attempts failed, a hopeless outcome was inevitable.

After the child was born, the delivery of the placenta was also left to nature, although the abdomen was often massaged to help matters along. If the placenta was retained, the midwife would pull on the umbilical cord. Rarely was manual removal attempted. The umbilical cord was tied with ordinary sewing thread about three or four inches from the child's abdomen. This length was believed to be important if one would prevent the child from having abdominal colic. Without any attempt for asepsis or sterilization, the cord was severed with the sharp edge of a piece of broken bowl or knife. The placenta was usually destroyed by fire. It was, however, considered an excellent remedy for tuberculosis when cooked with certain remedial herbs. But, as bad luck was supposed to follow the child if the placenta was thus used, this preparation constituted a very rare medicament.

Uterine hemorrhage was treated first by massage of the abdomen; then medicines were given prescribed by a physician. If the lochia suddenly stopped, medicines were asked of the physician and the patient was given pig's feet cooked with ginger as diet. Puerperal fever of any type was treated by cathartics; but when it became serious, it was a case for a physician.

Both mother and child were bathed after the labor with water in which ginger or the skin of Chinese grapefruit had been boiled. This was supposed to rid both mother and child of gas in the gastrointestinal tract. If there was an idol in the house, the water was placed before it for a blessing before it was used. Such a bath probably acts like a mild mustard bath would.

The mother's first meal was a bowl of rice fried with ginger in order to help her get rid of the toxic products accumulated both during pregnancy and during labor. The regular diet during the first month did not contain vegetables since these were thought to cause diarrhea in both the mother and the child. This was probably a survival of the custom in China where the soil in which vegetables are grown is most unsanitary. Vegetables were not provided because they were not recognized as necessary for a balanced diet. Salt fish, pork, chicken and duck were permitted. On the third day, the mother was given chicken cooked with the inevitable ginger to act as a carminative, to stimulate the digestive functions, and to increase the flow of milk. From the tenth day on, pig's feet cooked in black vinegar and raw ginger, without water were eaten for the same effects, also because they were less costly than chicken. After the first month, the mother was considered sufficiently recovered from the effects of labor and puerperium so that she could resume a regular diet, including vegetables.

Women from the southern parts of China favor foods which contain ginger and vinegar in combination; those from the north avoid them, and in their place use sugar in the mother's diet. The southerners avoid sugar and use ginger-vinegar combinations to stimulate the gastrointestinal tract and promote a better food assimilation. The northerners use sugar probably to add calories without much bulk to the diet. The selection of foods depends upon the customs prevailing in various parts of the country. This is merely a matter of common usage.

No special attention is paid to the woman during her puerperium. The poorer mother is compelled to return to her household duties as soon as possible. So a multipara may be up and about an hour or two after the delivery, although usually she is in bed between three and five days. The better classes can afford to let the mother take life more easily for a month. In any case, the mother cannot properly leave her house until a month after labor and the ceremonies for the baby have been celebrated. A "lucky day" is chosen, the baby is brought forth for a bath, his head is shaved, his ancestors are worshiped and then he is considered one year of age. Following this, there is a celebration and a banquet when chicken and red colored eggs are distributed to relatives and friends. After this, and not until then, the mother returns to her normal everyday social life.

That Chinese methods of life in San Francisco do not affect unfavorably the maternal or fetal mortality may be seen from the following figures taken from the San Francisco Board of Health records:

From January 1, 1929, to October 1, 1930, 649 Chinese women were delivered with three maternal deaths (0.47 per cent) and 13 stillbirths (2.0 per cent). Two of the women died in eclampsia and the other death was ascribed to embolism. One hundred eleven of the women were primiparous and 538 were multiparae. Of the 362 children born in 1929, 186 were males, and 176 females. There were two sets of twins in this series.

Of the 649 women delivered in 1929 and in 1930 up to October, 122 were delivered in the Chinese Hospital with one maternal death (eclampsia) and four children stillborn, one of which was from eraniotomy. The children in this series of 122 cases averaged 3,192 gm. in weight, the smallest being 1,927 gm. in weight and the largest child being 3,884 gm.

During the same period of time, January 1, 1929, to October 1, 1930, there were 38 deaths of children under one year of age of which 8 were due to prematurity, 2 were charged to congenital heart disease, and 2 to congenital debility. Thirteen died from pneumonia, 3 from tuberculosis, and 1 each from enteritis, convulsions, diphtheria, measles, whooping cough, etc., none of which could be charged to the labor.

The Chinese Hospital was opened on April 20, 1925, and until October 30, 1930, has had 230 deliveries. The records do not always record the position in the spontaneous normal deliveries, yet there are records of 9 breech, one face, and one transverse presentation. Two

placenta previas are recorded and one eclampsia. Operative interference was necessary 21 times (8.8 per cent), there being 16 low and midforceps, 2 high forceps, and 3 cesarean sections, without maternal death. The single maternal death was due to eclampsia (not delivered).

Thus one may see that the Chinese in San Francisco are delivered with a maternal and fetal mortality that is not unfavorable to them when compared with other quarters of the city. That this creditable showing depends in large part upon the fact that physicians alone superintend the deliveries is evident. Improvement in mortalities will follow more adequate prenatal care which now is limited, not because of racial customs and traditions but because of the expense at present attached thereto.

Bland, Goldstein, and First: The "Physiological" Anemia of Pregnancy. Surg. Gynec. Obst. 50: 954, 1930.

Of the 1000 patients examined in various periods of gestation, 47.4 per cent gave evidence of an anemia, with red cell counts of 3.5 million or less.

A distinct hemoglobinemia of 70 per cent or less occurred in 58.6 per cent of the gravidae. Only 24.7 per cent of the patients examined in the first two trimesters showed a moderate to a severe anemia, in contrast to 56.7 per cent of the patients examined in the third (rimester. Although the latter group constitutes a much larger number of patients, anemia is as a rule, more marked with the advance of pregnancy. Of a group of 35 patients with a definite anemia in the early months of gestation, 26 showed improvement at term.

Of 106 patients with a moderate to a severe anemia, 58.4 per cent began to show improvement within one to two days after childbirth. Of 94 patients with a mild anemia or a normal count during pregnancy, 73.4 per cent showed the effect of labor by a further reduction of the red cell count within twenty-four to forty-eight hours.

A marked improvement ensued within seven to ten days after labor, occurring in approximately 72.6 per cent of the 106 patients anemic during pregnancy.

The most interesting feature disclosed by this study was the remarkable recovery developing within two to six months after delivery. A distinct improvement in the red cell count took place in 92 per cent of the 100 patients examined. In 95 per cent there was also a marked improvement in the hemoglobinemia.

WM. C. HENSKE.

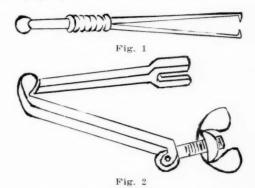
Society Transactions

NEW YORK OBSTETRICAL SOCIETY

MEETING OF MAY 12, 1931

DR. G. H. RYDER presented the following instruments: (1) A Uterine Packer for Cesarean Sections; (2) An Umbilical Cord Clamp.

The uterine-packer guide for cesarean section cases is an adaptation of an old instrument. This instrument is straight and four inches long, with a rounded knob at one end, and teeth with a sliding ring at the other. The teeth are caught in the gauze packing and fixed by the sliding ring. After the baby and the placenta are born, the opening in the cervix is located by the finger from above, and the packer guide is pushed through the cervix into the vagina. The uterine cavity is then easily packed. (Fig. 1.)



At any time after the completion of the operation, the packer-guide may be located in the vagina and removed with the attached gauze, or this may be pulled down within reach, and the packer-guide removed alone.

The umbilical cord clamp is made of bronze and nickel plated, it is in two parts joined at one end by a hinge. At the other end the lower part has a swivel thread and turn screw designed to fit into the forked end of the upper part. The cord is clamped with two long clamps and cut between. The baby is then removed, with one long clamp attached to a table, covered with a sterile sheet, and the umbilical cord clamp is adjusted on the cord, between the long clamp and the baby's navel. It is screwed down tight and the cord is cut through close on the distal side. The dressings are then applied around and over the clamp. The clamp may be removed at any time after five to eight hours, or it may be left on until the cord drops off. (Fig. 2.)

DR. HOWARD C. TAYLOR, JR., by invitation, read a paper entitled **Endometrial Hyperplasia and Carcinoma of the Body of the Uterus.** (For original article see page 309.)

DISCUSSION

DR. R. T. FRANK.—The uterine mucosa is constantly undergoing changes; eyelical mitoses are frequent, more so probably than in any other tissue in the

female except the breast. The reason, in my opinion, that breast carcinoma is so much more frequent in the female than in the male is because in the breast of the woman the same areas of tissue are undergoing these cyclical changes over a long period of years. In the uterine mucosa, on the other hand, in the majority of instances with every monthly cycle a large part of the mucosa is cast off, and, consequently, the stimulus is undergone at the next cycle by fresh areas of tissue. This, I think, saves the female from a greater incidence of adenocarcinoma of the fundus than would otherwise occur. Furthermore, I can add some physiologic evidence to prove that hyperplasia probably has a direct connection. I am not speaking now in the morphologic sense in which the practical pathologist is frequently forced to make a diagnosis between suspect tissues and carcinoma tissues, because I am a firm believer in Lubarsch's dietum that a given tissue is either carcinoma or is not. That does not signify that in a given instance we are justified in drawing conclusions from the picture under the microscope, or that we can invariably determine that this is malignancy or not; if the material is inconclusive sometimes time alone will show. Conclusive evidence that hyperplasia may be at fault is supplied by the fact that in a number of women long past the menopause, in whom carcinoma is found or suspected, to our great surprise (the number is still small because this was first an accidental find which we really are at present trying to confirm numerically without our opinion being definitely formed) the hormone content of the blood was found exactly as we find it in young menstruating women. This is an entirely anomalous finding and would, therefore, give confirmatory evidence to the fact that hyperplastic tissue in these old women is probably the basis of malignancy because as age advances irritated or activated tissues are much more prone to cancer symptoms or cancer change, whatever that may be,

DR. S. H. GEIST.—I was interested in the statement that there is a definite relationship between hyperplasia of the mucosa and the appearance of adenocarcinoma. We know that in hyperplasia of the intestinal mucosa, the so-called polyposis of the intestine, carcinoma is a very common sequel. However, it is to be remembered that the hyperplasia of the uterine mucosa is a very common lesion associated with many diseases of women and it is only natural that one would expect to find that a certain number of these women subsequently develop carcinoma. A curettage performed some years previously for conditions accompanied by hyperplasia of the endometrium might well have been done in a case that develops carcinoma subsequently without any definite relationship to the hyperplasia. Nevertheless the number of cases Dr. Taylor presented is somewhat significant, but I think in point of view of the frequency of the antecedent benign condition one must suspect that the malignancy may to a certain extent be coincidental.

The hormone finding of Dr. Frank in women past the menopause is significant, for in a study of postmenopausal bleeding in 180 cases, we found 8 per cent of women from one to more years past the menopause, there was a definite hyperplastic endometrium present.

DR. B. P. WATSON.—It is very essential in the training of any gynecologist or any surgeon, that he should study thoroughly the pathology of the various lesions.

I was going to make the same point that Dr. Geist made with reference to the frequency of hyperplasia and the difficulty of stating that because the woman had hyperplasia some years before and subsequently developed carcinoma, the one was necessarily the direct result of the other. We are coming to recognize that a very large number of women who suffer from menorrhagia have this cystic glandular hyperplasia.

The other point I should like to mention is in reference to some of those sections in older women where there was a carcinoma alongside an area, or in an area of mucous membrane where there were numbers of dilated glands. Now, that also

is a fairly frequent finding in older women. I wonder if Dr. Taylor were to take a series of sections from the uteri of women of similar age that he would not find just as many dilated glands in those where there was no carcinoma at all.

DR. J. A. CORSCADEN.-I regard the method of working back from carcinoma to the hyperplastic endometrium as extremely important. I think the other method of working from endometrial hyperplasia toward the carcinoma may perhaps also have some value. I have just completed a study of some 500 women who received an artificial menopause for fibroids and for bleeding. About half of them had hyperplasia. Out of the 500 there were two adenocarcinomas of the body. In one of them there was an atrophic endometrium found seven years before the carcinoma appeared, and in the other a polyp. She, by the way, had a second curettage in which a second polyp was removed. This follow-up period was from one and a half to seventeen years, averaging seven and a half years. If they had only been curetted, probably the findings would have helped more. Unfortunately, they all had sterilizing doses of radium, anywhere from 1,200 to 1,800 mg. hr., so that it is perfectly possible that the infant carcinoma was destroyed by this small dose of radium, but it is a significant fact that the two women who developed carcinoma of the body, one four years and one seven years afterward, did not have endometrial hyperplasia, except in one case where it was localized in an endometrial polyp.

DR. TAYLOR (closing).—I personally regard "precancerous" as a very useful term. It need not mean that cancer will certainly develop but indicates that the tissue is close to cancer in form. Subcancerous would perhaps be a better term. In any case some such word is of practical value to the pathologist who wishes to imply to the clinician that the case is one which deserves special consideration.

I was hesitant about making a definite statement in regard to the women over sixty years of age because hyperplasia has been regarded as a condition of earlier life.

In reference to the commonness of hyperplasia I am quite ready to admit that probably all women have minute areas of hyperplasia some time in their lives, just as they all have areas of chronic mastitis. The cases mentioned have, however, been those with symptoms of hyperplasia, and as such I believe they may be representative of cases in which the hyperplasia is particularly widespread. Of course I am quite willing to concede that any real statistical proof of a relation of hyperplasia to carcinoma is impossible.

Dr. Watson's statement about the glands being merely cystic and not hyperplastic is, I feel, a logical criticism. It was my impression, however, based upon my conception of the disease and of the tissue in the slides, that these glands were not merely dilated but were also hypertrophied.

Dr. Corscaden mentioned one case in which there was a polyp. I omitted any reference to polyps in the reading of this paper although I have studied over 50 cases. Reference in the published paper is to be made to several reported instances of the development of carcinoma from polyps, an occurrence having some bearing on the subject since many polyps are essentially localized areas of hyperplasia.

Dr. C. H. Peckham, of Baltimore, Md., presented (by invitation) a paper entitled **Chronic Nephritis Following Apparent Toxemia of Pregnancy.** (For original article see page 386.)

DISCUSSION

DR. E. E. BUNZEL.—I want to agree with Dr. Peckham in the difficulty in classifying these patients so far as the type of toxemia that they have is concerned. I think it is inadequate in many instances to try to classify them as mild, moderate

or severe. All we can really say is that they have toxemia or that they have convulsions with toxemia. We followed a series of cases for a period, examining them anywhere between ten and twenty-two months after they had been delivered, and in this toxic follow-up clinic we found figures very similar to those quoted by Dr. Peckham. We found in 37.6 per cent of our patients a blood pressure of 140 or over. We found 39.8 per cent of our patients had albuminuria. In doing an intravenous phenolphthalein test we found 54.2 per cent excreted less than 50 per cent of the dye. Of the cases which had eyeground changes, that is, papillary edema, retinitis or hemorrhages, 31 per cent showed persistent retinal changes.

We also followed these patients from the point of view of what happened to them in subsequent pregnancies and our conclusion was that if there had been a toxemia, mild, moderate or severe, or with eclampsia, they would have a 69 per cent chance, taking them all as one group, of a recurrence in a subsequent pregnancy; and with this recurrence they had only a 60 per cent chance of having a live child.

DR. A. W. BINGHAM.—I should like to ask in these cases which were toxic on the previous occasions what treatment was given to prevent their becoming toxic in the next pregnancy. I believe there is a relationship between a gain in weight and toxemia of pregnancy. I noticed that the weight was not given in any of these cases. I have found that if the patient gains over twenty pounds she is five times more likely to become toxic than a patient who has not gained twenty pounds.

DR. C. H. PECKHAM.—We are dealing with at least 50 per cent colored clinic material and our average patient we cannot persuade to come to us until seven or eight months, and they very much prefer to wait until they go into labor, and despite all our social service department has been able to do, we still have great difficulty in getting any patients to come in early in pregnancy.

In regard to the question of subsequent pregnancies, we have another series of eclamptic women in whom over 50 per cent in a pregnancy following the eclampsia showed some signs of a toxemic process.

Prof. E. C. Dodds, of London, England, presented (by invitation) a paper entitled **Biochemical Investigations in Obstetrics**.

BROOKLYN GYNECOLOGICAL SOCIETY

STATED MEETING, APRIL 3, 1931

DR. CHARLES W. MUELLER (by invitation) reported A Case of Fibroid Complicating Pregnancy.

This case is presented, not as a rarity, but to show the rapidity with which such tumors may grow and the rather unusual size that this tumor presented at subsequent operation.

J. S., aged twenty-four, presented herself at the hospital for the first time, via ambulance, having been transferred from a small sanatorium of this city. A primipara, at term, with ruptured membranes, in labor, having regular uterine contractures every fifteen minutes of forty-five seconds' duration. The membranes had ruptured the morning of admission with the onset of labor. She was admitted to the sanatorium where in the interval of several hours at least two vaginal examinations were done, and when it was found that a tumor complicated her pregnancy, she was transferred to the wards of Kings County Hospital, on the service of Dr. Duncan.

A brief history revealed a negative antepartum course as far as could be determined. There were no miscarriages, abortions or abnormalities of menses. Her past and surgical histories were negative. Physical examination revealed a patient in active labor with a normal temperature, pulse of 82, blood pressure 130/85. The abdomen was the size of a full-term pregnancy, the fundus of the uterus three fingers' width below the ensiform, lower pole head, floating at the brim. Back to the left, small parts to the right, upper pole breech. The fetal heart was heard in the lower left quadrant, rate 160, quality good.

Vaginal examination revealed a nulliparous outlet, edematous with a recent laceration of the perineum repaired with two chromic sutures. Slight bloody discharge. The cervix was soft, fairly well thinned out, and dilated three and a half cm. The membranes had ruptured. Posterior to the cervix, the finger encountered

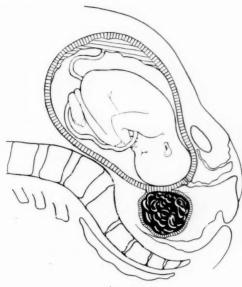


Fig. 1

a hard, firm, fixed, nontender mass, four and a half inches in diameter, which obstructed the descent of the head. The head was the presenting pole of the fetus which dipped into the inlet of the pelvis, but was not engaged. The symphysis was of normal width and thickness, the arch was ample as was the transverse diameter of the outlet. Four per cent mercurochrome was instilled into the vagina. The diagnosis was pregnancy at term, with fibromyoma of the uterus, occupying the hollow of the sacrum and thus preventing the head from descending in the normal manner.

The blood count showed red blood cells 3,168,000; hemoglobin 78 per cent; white blood cells 25,400, with 86 per cent polymorphonuclears.

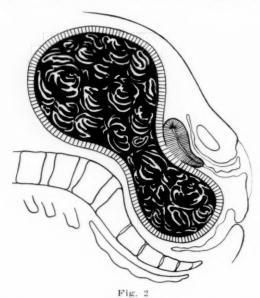
The x-ray examination showed pregnancy at term, cephalic presentation, occiput being directed to the left and anteriorly, but relatively high in the pelvis.

A cesarean section was done of the usual low cervical cross-flap type. The mass described in the vaginal examination was found to be a fibromyoma four inches in diameter, intramural, arising from the lower posterior segment of the uterus, but it was deemed inadvisable to remove either the tumor or the uterus at this time because of the loss of blood, the added surgical shock, the risk of infection because of the previous manipulations prior to her admission to our institution.

The child weighed seven and a half pounds and was resuscitated easily. There was a spina bifida in the lower lumbar region.

The postoperative course was uneventful except for a slight superficial skin infection.

From her discharge on March 2, 1928 until March 14, 1930, two years later, no contact could be made with this patient. At this time, she was admitted to St. John's Hospital with the chief complaint of progressive enlargement of the abdomen, pain while standing and walking. The patient noticed that, following the cesarean section, her abdomen steadily increased in size but except for disfigurement and a slight discomfort, it caused her little or no trouble, and rather than subject herself to operation, she waited until the present time. During the past six to eight months, she had noticed a frequency of urination without pain or burning; also had suffered considerable pain which she described as in her pelvis, such as a bearing-down feeling while standing or walking. Bowels were regular. There had been no



change in her menses, the same as before her cesarean and previous to the enlargement of her abdomen.

The physical examination showed a stout female adult, aged twenty-five, not apparently ill. Pulse rate 80 and strong. Blood pressure 125/82. Abdomen larger than the size of a full-term pregnancy, smooth in outline. There was a large, hard, firm, nontender tumor mass, filling the abdomen to within three fingers' width of the ensiform. It was not freely moveable, but none of the physical signs of abdominal fluid could be determined.

Vaginal examination showed the external genitalia normal. The examining finger could only enter the vault of the vagina for a distance of one inch, when it encountered a hard, large, firm, nontender mass which occupied the entire pelvis, pushing a very small cervix well forward just behind the symphysis. Nothing else could be determined.

The laboratory findings were: Red blood cells, 4,720,000, hemoglobin 80 per cent, white blood cells 8,650, polymorphonuclears 60 per cent. No change in morphology. The bleeding time was two minutes. Coagulation time was six and a half minutes. Sedimentation time was eighty minutes. Blood chemistry showed sugar 100, urea 30, creatinine 1.2.

The patient came to operation several days after admission. A mid-line incision was made from the symphysis to within three or four inches of the ensiform. Pathology, an immense tumor, retroperitoneal in type, springing from the pelvis, filling almost the entire abdomen, larger than a nine months' pregnancy, firm, very slightly irregular in outline with a large nodule filling the pelvis, lying posteriorly to the uterus. The uterus was slightly smaller than normal. Its appendages were negative with tubes patent.

The tumor was delivered through the abdominal wound, its peritoneal layer opened just above the fundus of the uterus and the fibromyoma was removed by blunt dissection. The oozing was controlled by packing lap sponges and a hot five-yard roll of gauze into the denuded area. The peritoneum was closed by continuous plain suture. The abdominal wall was then closed in layers, by the usual manner.

Postoperatively, there was a slight morbidity. The wound healed by primary union. There was no difficulty encountered by hemorrhage, shock, distention or vomiting. The sutures were removed on the tenth day. However, on the fourteenth day, the patient complained of pain in the lower left extremity. Some edema and slight tenderness were noted on the inner surface of the left thigh and calf. There was slight tenderness also over the lymphatics of the groin. Diagnosis was thrombophlebitis of the long saphenous vein. This, however, cleared up rapidly and the patient was later discharged in excellent physical condition.

The tumor mass weighed twenty-seven pounds. The microscopic diagnosis was fibromyoma without evidence of degeneration.

Examination two months postoperatively showed the uterus in good position, normal size, freely moveable, not tender. The adnexa were palpable and thought to be normal.

- Dr. Samuel Lubin presented a report of a case of **Double Monster**, **Ischiopagus**. (For original article, see page 422.)
- Dr. B. P. Watson read (by invitation) a paper entitled **Pregnancy** and Labor Complicated by Fibroid Tumors. (For original article see page 351.)

DISCUSSION

DR. HARVEY B. MATTHEWS.—The incidence of fibroids in Dr. Watson's experience is about the same as it has been in ours, about 1 to 1½ per cent. In the last 6,000 cases at the Methodist Episcopal Hospital, there were twenty cases of fibroids complicating labor. Of the early cases up to the twenty-eighth week, there were 15 with fibroids, these being mostly abortions and premature labors. Of the twenty cases at or near term, 8 were spontaneous, 11 were forceps deliveries, one had a classical cesarean section. At the Long Island College Hospital in two years, among 1,985 deliveries, there were 17 cases of fibroids complicating labor, of which 12 were spontaneous, 3 forceps and 2 cesarean section. This again shows that these fibroids do, in the majority of cases, get out of the way of the presenting part and delivery takes place either spontaneously or with ordinary obstetric help. At the Coney Island Hospital, over a period of about fifteen months, we have delivered 1,020 cases without a single case of fibroid complicating pregnancy at or near term. So that we have a total of 9,000 cases with an incidence of fibroids at or near term of 1 in 244.

In the operative treatment of these cases Dr. Watson spoke of myomectomy versus hysterectomy, or rather, myomectomy in certain types of cases, and hysterectomy in other types. It seems to me that unless you are anxious to save the woman's

uterus for a subsequent pregnancy, hysterectomy is a better operation than myomectomy in the presence of fibroids.

DR. GORDON GIBSON.—In talking to students I like to boil it down somewhat in this fashion: Given a woman who has a fibroid and has become pregnant, there are four problems to contend with. The first of these is: What is the fibroid going to do to the pregnancy? The second is: What is the fibroid going to do to the labor? The third is: What effect is the fibroid going to have upon the puerperium because we know that fibroids do interfere with drainage of the uterus. They also interfere with involution of the uterus and at times we have very serious after effects as a result. The fourth and last problem to be considered is: What does the pregnancy do to the fibroid?

DR. ALFRED C. BECK.—At the Long Island College Hospital we have learned in the last ten years to be conservative. We do not operate as soon as we used to. The labor we have learned is prolonged if the woman has many fibroids in the uterus, even though they offer no obstruction. The uterus does not contract as it should. We have also learned in possibly a half-dozen cases that large fibroids in the lower uterine segment below the head are pulled up as the cervix dilates. That is particularly true when they are in the anterior or lateral aspect. If they are in the posterior wall, they are not pulled up, and we seldom allow those cases to have any labor. Formerly when a cesarean section was indicated, we did the classical operation and left the uterus, so we have had some experience with fibroids that were left behind. We learned, unfortunately, that very frequently these fibroids interfered with drainage and the convalescence is accompanied by considerable morbidity, and we had several deaths that we though might have been avoided had we done a hysterectomy or myomectomy. Personally, I never have done a myomectomy at this time. We have also observed in patients who delivered spontaneously or who delivered from below, that these fibroids frequently interfered with drainage and if they were infected, the course was a very serious one. Several of our patients died from puerperal infection, even though they delivered and pulled these big fibroids out of the pelvis, and we feel that had we operated upon them, done a hysterectomy or possibly a myomectomy, their lives might have been saved.

DR, RALPH M. BEACH.-When you feel a pedunculated fibroid in the culdesac it is interesting to know where the fibroid springs from. I have had two cases within the last three or four years. One woman was in the early months of pregnancy. She suffered from very severe pain, and we felt a small pedunculated fibroid in the culdesac. We attempted to treat her conservatively with rest, but despite this the pain increased, and when we operated upon her we found that this pedunculated fibroid sprung from the anterior uterine wall, going around the right adnexa, and was in the culdesac. She had another tremendous fibroid in the upper segment and in that case it seemed inadvisable to leave the uterus. In another case where a pedunculated fibroid was in the culdesac, the patient went to six months with practically very few symptoms. It looked as though it was going to be one of those cases that we could carry along and possibly get the tumor out of the pelvis or get her near enough to term so as to deliver a live baby. At about six and a half months she had very severe pain, the tumor became very tender, we could feel liquefaction through the culdesac, and operation was decided upon. On preliminary examination we thought the tumor sprung from the lower part of the posterior wall. On operating we managed to shell this tumor out of the pelvis and found that the pedicle came from a point within about two inches of the fundus on the posterior wall. In that case we removed the tumor,

but unfortunately about forty-eight hours later the patient developed intestinal obstruction and we had to go in again and relieve adhesions and do a hysterotomy at the same time. She made a good recovery and now is pregnant within three weeks of term.

I think the important point brought out by Dr. Watson and which has been emphasized by Dr. Beek and Dr. Matthews is that every time fibroids become tender, this is not an indication for operation and in the past many operations have been done unnecessarily. However, I believe a fast sedimentation time is an indication for operation.

DR. ABRAHAM KOPLOWITZ.-We have seen a good many fibroids on Dr. Mills's service at the Kings County Hospital that were not large enough to interfere with labor. I have always been under the impression that they will involute the same as the uterus will without giving trouble subsequently. Being impressed with that, in taking care of a case something less than a year ago in a woman who had been under my care during the whole course of her pregnancy, but who for some reason or other did not show up in the last four or five weeks when I felt as if I should make one vaginal examination, I entirely missed a large fibroid that had been in the culdesac all the time. She came into the hospital and the intern reported to me that the head was pretty low down, but he could not make out dilatation. On my first rectal examination I could not make out anything. I decided to do a vaginal examination and found the cervix way up under the symphysis and a large fibroid occupying the pelvis. There was only one thing to do and that was a cesarean section. I discussed with her the possibility of a hysterectomy and she asked that if possible the uterus be left in as she did not want to be left with one baby. I did a two-flap operation without any difficulty. The fibroid I found to be subperitoneal and large. I felt that myomectomy would be a comparatively difficult operation and with the idea of waiting for retrogression and making a much easier operation subsequently, I left it in. I saw that woman four months postpartum and at that time I am sorry to say I hardly noticed any change in the size of the fibroid. The question that bothered me was whether I played the part of safety for the patient by leaving that tumor in at the time and not adding any more difficulty to her cesarean section or whether it would have been wiser to remove it.

DR. SAMUEL A. WOLFE.—Dr. Watson has confirmed the observations made in our laboratory, that fibroids of any appreciable size accompanying pregnancy undergo edema or red degeneration with subsequent liquefaction necrosis.

Why so many degenerated fibroids do not produce any clinical picture, even in instances where the tumors are subperitoneal, is yet to be determined. Tumors which have undergone red degeneration and liquefaction necrosis have been noted to grow in a succeeding pregnancy. This is difficult to explain in the light of the necrosis of the tumor.

DR. B. P. WATSON.—The question was raised as to the advisability of performing myomectomy at the same time as the cesarean section. We cannot lay down any general rule that will apply to all cases. In a woman over thirty-five years with multiple fibroids in the uterus I should nearly always do a hysterectomy, but in a young woman auxious to have more children, I think myomectomy is justified and in our hands has given satisfactory results.

In regard to the future history of those patients, I am one of those who believe that the dictum, "Once a cesarean always a cesarean" does not hold; that when cesarean section has been done and the uterine wall has been properly sutured, it is in most instances as strong as ever, if the convalescence has been afebrile. We have all had the experience of examining uteri some time after cesarean section and have found the same thing, namely that it is very difficult with the naked eye and even microscopically to find the old scar. The same applies to the bed of a tumor after the operation of myomectomy. If we shell the tumor out and bring the wall together in layers, the wall at that part is as strong as any other part of the uterus. So I have no hesitation in allowing a patient to go through labor after myomectomy or after a cesarean section which has been done for some condition other than a contracted pelvis. I think we may be inclined to be too apprehensive of labor in such cases.

In the present series we did not happen to have any case in which a tumor of any size entirely disappeared, but unquestionably it does occur.

I do not know of any definite clinical sign which will tell us when these tumors are liquefied. It is a perfectly aseptic process. There is a slight degree of leucocytosis during the period of pain and tenderness, it is never marked, and we have not noted any change in the leucocyte count or in the sedimentation time in those cases where liquefaction has taken place. After all, this process of necrobiosis is an aseptic one and even when the tumors are broken down there appear to be no general symptoms. Pain and tenderness tend to disappear after the liquefaction takes place.

Dr. Wolfe asked whether these liquefied tumors might grow again in subsequent pregnancies. That I cannot answer categorically. I think possibly we imagine that those tumors are getting bigger during pregnancy simply because they become more easily palpable, especially the subserous ones.

The enucleation of retroperitoneal tumors, is usually easy when it is done at the time of cesarean section. The tissues are all loose and opened out and, in my experience, there has been less bleeding and less difficulty in shelling them out than when it is done in a nonpregnant patient. I did meet with one case where I thought we were dealing with a retroperitoneal fibroid growing from low down in the cervix. I very quickly gave up the attempt on finding that it was not a fibroid growing from the uterus, but a fibroma growing from the lateral pelvic wall.

CHICAGO GYNECOLOGICAL SOCIETY

STATED MEETING, APRIL 17, 1931

Dr. Alexander G. Gabrielianz described a case of Fibroma of the Ovary.

L. C., seventy years of age, white, widow. She had had eleven children; eight now living. Her pregnancies were all normal and deliveries were without instrumental interference. At the age of thirty-seven she had a miscarriage at seven months from unknown cause; after the sixth delivery the patient had puerperal sepsis and remained in bed forty days. The only history of illness was typhoid fever at the age of fourteen.

Menstrual history normal. Climacterium at fifty-five. Her last menstrual period was abundant and lasted seventeen days. She had not lost any weight.

The patient complained of a sudden pain over the entire abdomen followed by gradual enlargement of the abdomen. I first saw the patient twelve hours afterward, at which time the pain was more severe. She had had no bowel movement but she urinated normally. On questioning the patient stated that she had had a similar pain twelve years ago but her abdomen was less distended. She was confined to her bed for one day at that time.

On physical examination the abdomen was found distended, tender, and tympanitic. Several soapsuds enemas administered without result. After transfer to the hospital, another enema given but with the same unsatisfactory result.

I then gave the patient spinal anesthesia, to relieve the abdominal distress by relieving the meteorism, and in order to examine the patient further. Shortly after spinal anesthesia with spinocaine, visible peristalsis started and the patient expelled gas, partly by rectum and partly by eructation. The abdomen became much softer and a tumor mass was easily palpable about four fingers' width above the symphysis and about two inches from the midline on the left side. The mass was the size of a small grapefruit, irregular in shape, with a smooth surface, of hard consistency, movable from side to side downward and with limited mobility upward.

Vaginal examination showed the uterus small, retroflexed, firm, not freely movable, not tender, and the surface was smooth. Adnexa were not palpable. The culdesac was free.

On bimanual examination I could find no relationship between the tumor mass in the abdomen and the uterus, partially due to the meteorism which was still present in a lesser degree, and partially due to the limited mobility of the uterus.

Because the patient had had some relief from the spinal anesthesia, I postponed interference until the following morning, when she was operated upon under spinal anesthesia, using 3 c.c. of spinocaine. Previous to the operation an injection of 1 c.c. of 5 per cent ephedrin hydrochloride was given.

A midline abdominal incision was made and the tumor mass on a long twisted pedicle was delivered with ease and the operation completed by putting one forceps on the pedicle followed by ligature and peritonization of the stump. The uterus showed no cicatrix. The abdomen was closed in the usual way. The postoperative course was uneventful.

Macroscopic Examination.—Size $12 \times 9 \times 6$ cm. Consistency hard. The tumor was firmly attached to the ovary, which was the size of an English walnut, cystic and contained cheeselike masses. Attached to the ovary and the size of a small navel

orange was a cyst filled with bloody serous fluid. The large stump of the pedicle was black and twisted. The left fallopian tube was apparently healthy but was deeply injected and dark in color.

Diagnosis before operation was not certain but we considered intestinal obstruction. The condition appeared to be a detached uterine fibroid which attached itself parasitically to the left ovary. On further examination of the specimen it was found to be a fibroma of the ovary. This was proved by microscopic sections which showed a mass of hyaline fibrous tissue of a mature type with a few small areas of mononuclear infiltration, the usual interlacing bundles of fibrotic-like tissue being the predominant tissue. Certain areas showed beginning calcification. There was no evidence of any unusual cellular activity of a malignant nature present. The whole picture was that of a benign slow-growing fibroma of the ovary.

Dr. Lester E. Frankenthal, Jr., and Dr. Alfred J. Kobak reported a case of Trichomonas Vaginalis Occurring Before Menstruation.

The patient, aged twelve years, had never menstruated, came to the Michael Reese Hospital on February 20, 1931. Examination revealed reddened genitalia bathed in a frothy, purulent discharge. A hanging drop examination showed many motile flagellates and routine uranalysis by the laboratory showed many Trichomonas vaginalis. Subsequently we catheterized her and found negative urine both by hanging drop and culture, according to the method of Stein and Cope. A stool examination was likewise negative. Cultures of vaginal secretions yielded a heavy growth of trichomonas. Due to the age of the patient and the intact hymen, the usual vigorous treatment was not undertaken. However, the first month the patient received weekly applications of 5 per cent silver nitrate with daily instillations of 2 per cent mercurochrome. During the next four weeks we substituted daily astringent douches for the mercurochrome instillations. At the present time hanging drop examination still reveals numerous trichomonas and the treatment has not been very successful.

Dr. W. C. Danforth presented a paper entitled The Treatment of Occipitoposterior Position With Especial Reference to Manual Rotation. (For original article see page 360.)

DISCUSSION

DR. D. S. HILLIS.—Although manual rotation is the procedure of choice in cases of occipitoposterior position we also need something in place of manual rotation and this, in my opinion, is the Kjelland forceps. These are not generally used and have gotten into bad repute on account of the large circle that must be described by the handle in order to rotate the head on its long axis. It is a hard thing to do and requires an expert to do it accurately without injury. With the bayonet-shaped forceps this rotation is done with more ease and less danger.

DR. E. L. CORNELL.—I should like to eall attention to a method of rotating the posterior head which I described several years ago in an article on forceps. In the left posterior position you use your right hand, while in the right position you use your left hand. Fit the fingers into the upper lambdoid suture and with the pain push the head forward in an upward circular manner toward the pubis, using the lambdoid suture as a lever. A large percentage of these cases will rotate in this way. In most cases, it is a mistake to push the head up and disengage it before making an attempt to rotate it in this manner. It is very sur-

prising the ease with which this procedure is accomplished. After the head is rotated you may allow the patient to go on and deliver or you may apply forceps.

I agree that the anesthetic of choice is ether.

DR. R. W. HOLMES.—It is well that Dr. Danforth did not mention the Scanzoni maneuver for the correction of the malposition. At times, it may be absolutely necessary, but the manual correction is so far superior, and so much safer, as an obstetric procedure, that the latter always should be first attempted. The dangers of injury to the head, and the likely serious mutilation to the maternal soft parts should condemn it. The Kjelland forceps alone should be considered if one must use the Scanzoni procedure. I concur with Dr. Danforth in condemning the procedure of instrumental rotation.

Once in a while, after rotation the head will return to the primary position. In that event it is necessary to pass the hand into the uterus after the cephalic correction, grasp the shoulder and rotate the trunk to an anterior position, then impress the head into the brim.

Dr. Emil Ries read a paper on the **Colposcope** with particular reference to the use of the instrument in the detection of early cancer of the cervix. (For original article see page 393.)

DISCUSSION

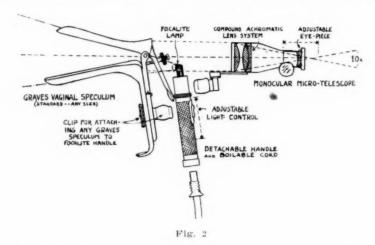
DR. RICHARD A. LIFVENDAHL.—Undoubtedly the instrument opens up a wide field for study in order to correlate what is seen through the instrument and



Fig. 1

what the pathologic findings are. Also, it serves to concentrate our attention on the cervix in a more detailed and systematic fashion. Its use should not be confined to the occasional patient in whom we suspect some pathology but should be used routinely in order that we have a better understanding of changes in this region and especially for the detection of early carcinoma. After using the colposcope for a short time I felt that the instrument could be simplified and its expense decreased. The first part of the equipment to consider is the stand which is somewhat cumbersome, heavy, and rather expensive. The second problem was whether binocular vision was really necessary, for we know that in detailed microscopic work many pathologists prefer monocular scopes. With the aid of the Cameron Surgical

Company the instrument demonstrated in the photographs was constructed. (Figs. 1 and 2.) The advantages herein seen are, that it can be attached to any Graves speculum, is very compact, and should be much less expensive. The blades of the speculum in the sample are black plated on their inner surfaces in order to decrease the amount of light reflection. The ordinary 110 volt current is cut down by a rheostat and the cord is detachable from the handle. Another advantage is that



the optical system can be rotated out of, or removed from the orifice, which leaves an excellent light in the vagina with which one can carry out therapeutic or diagnostic procedures on the cervix or vaginal walls. As the instrument is constructed at this time our field is about three-quarters of that which the Hinselmann scope gives and in addition we do not have the stereoscopic type of optical system which does afford some advantages. However, I feel that the tele-vaginalite will be of great help to us in the earlier diagnosis of cervical lesions.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

REVIEW OF NEW BOOKS

OBSTETRICS

A lay publicist presents1 to lay women a discussion of the Gwathmey method of obstetric colonic analgesia. There is little to criticize in her presentation of the development of the method, the testimony of physicians, or the testimony of patients regarding the benefit of the procedure, except that a few of the letters quoted are rather fulsome in their praise. The remarks on elective version might have been omitted. No one method of lessening pain in labor is applicable to all cases, and elective version, inhalation anesthesia, and various means of producing "twilight sleep" all have their place.

Propaganda of this sort is useful in opening the way to similar popular discussions of other health problems of women, for instance, cancer prophylaxis.

-Philip F. Williams.

What the Public Should Know About Childbirth2 is designed for the laity but contains much of interest to the profession as well. A short simple history of obstetrics introduces the main topics. Some of the subjects dealt with are superstitions and customs, twilight sleep and its disadvantages, gas-oxygen anesthesia, on the other hand, being favored. The Catholic viewpoint is emphasized throughout, with its influence on the teaching and practice of obstetrics. The writer quotes innumerable authors in such detail that it is frequently disturbing to the reader and interferes with the continuity of the text.

-R. T. Frank.

ENDOCRINOLOGY

The ninth installment of the second volume of the Handbuch der Inneren Sekretion3 has just appeared. It contains two subjects, the main one dealing with senility and rejuvenation, which occupies nearly 250 pages and contains much of general interest. It is written by Romeis of Münich.

The thyroid gland in old age undergoes fibrosis (senile atrophy). In the parathyroid, on the other hand, there is an increase in lipoid in the parenchymous cells and connective tissue. The same changes are noted in the hypophysis. The adrenal shows simple senile atrophy. In the testis few changes are noted irrespective whether libido disappears or remains. The ovary of mammals in senility contains a few follicles but no corpus luteum.

¹Easier Motherhood. By Constance L. Todd. New York, The John Day Com-

pany, 1931.

²What the Public Should Know About Childbirth. By Walter B. Gossett, M.D., The Midwest Co., Minneapolis, 1931.

³Handbuch der Inneren Sekretion. Herausgegeben von Dr. Max Hirsch. II Band. Lieferung 9. Curt Kabitzsch, Leipzig, 1931.

Vasoligation has proved to give both satisfactory and unsatisfactory results. Other technics with the same object in view including transplantation, are described. Such gonadal transplants rarely survive after four years. The illustrations accompanying this article are good and the literature is dealt with in a fairly satisfactory manner.

Twenty-five pages are devoted to the endocrine aspects of stature and body configuration. This chapter is written by Rautmann of Braunschweig. It is the mesodermal tissues which are mainly influenced by hormones. Therefore the effects are observed in the skeleton, muscles, vascular, genitourinary systems as well as the corium and subcutis. As an index the author uses the body length contrasted with chest circumference and head measurements. The thyroid, prepituitary and gonads are most likely to affect configuration. The article is clearly written but extremely summaristic.

-R. T. Frank.

The second edition of Cotte's book on the Functional Troubles of the Female Genital Apparatus' has appeared three years after the first edition, bespeaking its appeal to the medical profession. This voluminous treatise features both the physiologic and clinical aspects. While on the whole the physiology is presented in a most careful, scholarly fashion, the clinical portion occasionally suffers from lack of critique and acceptance of very doubtful data.

The ground covered is formidable. Nothing but a very brief summary can be given. Chapter I deals with the sex cycle in mammalia. Chapter II, which has been added in this edition, considers the disturbance incident to ovulation. Chapter III details the morphologic and functional changes occurring in the tube, vagina, and mammary gland during the sex cycle. Menstrual disturbances are dealt with in Chapter IV. Chapter V discusses the various troubles incident to copulation, perversion, etc., while Chapter VI takes up impregnation, nidation and disturbances of the ovum after impregnation, as well as artificial insemination. Chapter VII deals with the secretions of the genital tract. Chapter VIII covers the circulation of the blood. Chapter IX describes the innervation and its disturbances, and includes operations on the pelvic sympathetic system. The final chapter deals with ovarian insufficiency and eastration symptoms.

From this it will be seen that the material dealt with is huge. Unlike many similar books, it impresses by its earnestness, scientific point of view, and surprising knowledge of the world's literature. Because of the real value of the book, I take occasion to point out a few minor details such as inaccuracy in ascribing discoveries to the wrong individual. For example, "folliculin" is noted as discovered in 1928 although I had described its physiologic activity in 1922. The reaction of the female sex hormone upon the cervical glands is credited to Kennedy although it was really published several years before by Pick, Faure and Dohrn. The author doubts the presence of female sex hormone in all but the most recent corpus luteum, although it has been definitely shown, particularly by Allen, that the human corpus luteum contains large quantities of hormone.

Some of the therapeutic measures recommended by the author will certainly eventually require revision. He claims to obtain good results in inducing ovulation by means of prepituitary extracts although as yet the tests performed on all available extracts have proved negative. Likewise his use of antisyphilitic treatment for intermenstrual pain seems unjustified unless a positive Wassermann is noted. Neither can I agree with unilateral castration for this troublesome symptom as I have too often seen patients who were operated upon for this reason, within

^{&#}x27;Troubles Fonctionnels de L'Appareil Genital de la Femme. Par Prof. Gaston Cotte. 2e Edition. Masson et Cie, Paris, 1931.

six months or a year showing the same symptoms on the opposite side. Insulin as a treatment of menorrhagia has likewise not proved effective in most hands.

In spite of some of these minor defects, I may repeat that this book, lavishly illustrated, with an enormous bibliography, and containing in its pages many of the original investigations of the author, is worthy of careful study by all gynecologists.

Haberlandt's first monograph on this subject was published in 1919. The present monograph⁵ is a summary of the preceding one together with additional experiments performed in the interim. According to the author, transplants of the ovaries of pregnant animals cause temporary sterility in the experimental animal. He was also able to sterilize rabbits with injections of "ovarial opton" prepared according to Abderhalden's method, from the ovaries of pregnant cows, or with "placental opton." This is in sharp contrast with ovarian opton from nonpregnant animals. Fed by mouth this same preparation gives results which are less striking. No bad effects are noted in later pregnancies. The sterilization is effective in rabbits up to three months. He is now ready to try the method clinically with these same preparations.

The literature covering the subject is carefully gone into and utilized to strengthen his thesis. No experimental data are given in this monograph which, on the whole, is not extremely convincing.

-R. T. Frank.

MISCELLANEOUS

Biesenberger's monograph⁶ deals with the deformities of the breast and the cosmetic operations devised for their repair. He has found that a considerable number of women, particularly those of the socially higher ranks and those engaged in active sports, desire to have such disfiguring changes repaired. The types of breasts found are the pendulous, the adipose, and the asymmetrical. In addition, occasionally marked hypertrophy of the breasts likewise requires intervention, Of operations available, amputation, a radical measure; mastopexy, skin plastics, and resection methods are at the disposal of the surgeon. A number of operations are described, including a rather complicated resection of his own devising. This monograph is profusely and adequately illustrated.

-R. T. Frank.

Moeneh's Studies on Fertility represent a large amount of experimental work performed under a grant made by the National Committee on Maternal Health. It represents the material of 141 intensively studied cases and 60 additional cases not as yet fully worked up.

Instead of being satisfied with the ordinary sperma examinations, the minute characteristics of the sperma have been studied by new methods largely developed in connection with studies performed by the veterinarian, W. W. Williams, as well as Dr. Savage, which have proved of much benefit to the breeders of cattle.

Moench emphasizes that there are intermediate grades between sterility and fertility until the lowest grade of fertility merges into clinical sterility. He feels that in women, abortion and repeated premature births are evidence of minor re-

⁵Die hormonale Sterilisierung des weiblichen Organismus. By Dr. med Ludwig Haberlandt. Verlag von Gustav Fischer, Jena, 1931.

⁶Deformitäten und kosmetische Operationen der weiblichen Brust. By Hermann Biesenberger. Verlag Wilhelm Maudrich, Wien., 1931.

⁷Studien zur Fertilität. By Prof. G. L. Moench. Ferdinand Enke, Stuttgart, 1921. 1931.

duction in fertility, put are clinically not definable. In the male, however, intensive study of the sperma cannot only show fertility, but also the degree of fertility of the individual. It should include not only the number and the motility of the spermatozoa but their morphology and the biometry of their head lengths as well. He warns against temporary or accidental reduction of motility. On the other hand, the morphology and particularly the size of the head of the spermatozoon, is most useful in grading the impregnation power of the sperma. In no instance was good male fertility found in men whose sperma showed more than 20 per cent of abnormal spermatozoan heads. This is a most valuable contribution to fertility studies.

-R. T. Frank.

Books Received

COURTS AND DOCTORS. By Lloyd Paul Stryker. New York, The Macmillan Company, 1932.

FEMALE SEX HORMONOLOGY. By William P. Graves, Professor of Gynecology at Harvard Medical School, etc. Illustrated. W. B. Saunders Company, Philadelphia, 1931.

SURGEON GENERAL OF PUBLIC HEALTH SERVICE. Annual Report for the Fiscal Year 1931. United States Government Printing Office, Washington, 1931.

MAN AND WOMAN IN MARRIAGE. By C. B. S. Evans, Member of Faculty of Northwestern University Medical School, etc., With an introduction by Rudolph Wieser Holmes. Chicago, Bruse-Roberts, Inc., 1931.

ERGOT AND ERGOTISM. By Dr. George Barger, Professor of Chemistry in University of Edinburgh. London and Edinburgh, Gurney and Jackson, 1931.

SEX HOSTILITY IN MARRIAGE. By Dr. Th. H. Van de Velde. Translated from the German. New York, Covici, Friede, 1931.

MEDICAL REPORT FOR THE YEAR 1930. Glasgow Royal Maternity and Women's Hospital. Glasgow, 1931.

CAESAREAN SECTION, an Analysis of 352 Consecutive Cases, etc. By Frances Ivens-Knowles, Clapham Maternity Hospital, London. J. & A. Churchill, London, 1931

DIE PFLEGE DER FRAU. Von Professor Dr. Ludwig Adler, Zweite Auflage. Wien. Franz Deuticke, 1932.

WECHSELJAHRE DER FRAU. Von Geh. Rat Professor Dr. Hugo Sellheim, Universitaets Frauenklinik in Leipzig. Stuttgart, Ferdinand Enke, 1932.

DEPISTAGE DE LA SYPHILIS en Practique Obstétricale. Par P. Rudaux, Accoucheur, Maternité de Paris, et H. Montlaur, Assistant de Syphiligraphie, Maternité de Paris. Masson et Cie, editeurs, Paris, 1931.

RADIOTHERAPIE. Par Ch. Guilbert, avec la Collaboration du Dr. Jean Quivy. N. Maloine, editeurs, Paris, 1932.

LES LÉSIONS CEREBRO-MENINGEES A LA NAISSANCE. Par Robert Waitz, Ancient Interne des Hopitaux de Paris. G. Doin & Cie, editeurs, Paris, 1931.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

Pathology of Pregnancy

Cabanes, P. A.: A Simple Treatment of Hyperemesis Gravidarum. Bull. de la Soc. d'obst. et de gynée. 6: 420, 1930.

Eleven cases of hyperemesis gravidarum are reported by Cabanes in which cures were obtained by either the production of fixation abscesses or the injection of aseptic pus. In all the cases the vomiting subsided rapidly after the injections and the pregnancy continued unmolested in all cases but one where typhoid fever was present. The author, however, does attach great importance to the diet which is as follows: restriction of fluids, frequently repeated small meals composed of purées of vegetables and fruit, and glucose injections to prevent dehydration.

J. P. GREENHILL.

Aburel, E.: Considerations of the Pathogenesis and Treatment of Vomiting in Pregnancy. Bull. de la Soc. d'obst. et de gynée. 7: 34, 1931.

The author's conception of the mechanism of vomiting during pregnancy is as follows: In a nervous, spasmophilic and susceptible individual, the irritation of the uterus during pregnancy produces an uterogastric reflex. The uterus incites a spasm of the pyloric portion of the stomach and vomiting results. The author says he verified his idea of the pathogenesis of vomiting in pregnancy by therapeutic results which he obtained by anesthetizing the centripetal path of the uterus. By anesthetizing the lumboaortic plexus one may give a woman who has not been able to keep any food in her stomach, a large meal which will be well tolerated. Two cases are reported in which complete cures were obtained after two anesthesias.

J. P. GREENHILL.

Saenger, H.: Death From Hyperemesis Gravidarum. Arch. f. Gynäk. 142: 152, 1930.

The author reviews at length the history of hyperemesis gravidarum and gives a résumé of all the 33 cases in the literature, which ended fatally. He also adds one case of his own. An analysis of the reported cases leads Saenger to conclude that pregnancy should be terminated promptly for continuous and uninterrupted vomiting, especially when lasting more than one week with a pulse above 96, marked loss of weight and weakness. The interruption should be done, if at all, before the ninth week of pregnancy as all the reported deaths occurred after the ninth week. The development of neuritides, pyrexia, or icterus are forebodings of serious pathologic changes and clearly indicate prompt interruption of the pregnancy. The negative chemicophysical findings are of no value in the prognosis. The development of fever, or of cerebral changes such as apathy, delirium, etc., are evidences that the proper moment for interruption has already passed.

RALPH A. REIS.

Willibald: Menstruation-like Hemorrhages During Pregnancy. Monatschr. f. Geburtsh. u. Gynäk. 85: 233, 1930.

Literature offers many instances of the occurrence of menstruation-like hemorrhages during pregnancy. Willibald studied the histories of 2,800 pregnant women and found that 20 of them (0.7 per cent) had such hemorrhages. From this study and the reports in literature, he concludes that the mild hemorrhages which occur during pregnancy at the time a patient would menstruate if she were not pregnant are not true menstrual periods. They have no significance in the determination of the day of confinement. However, if the amount and duration of bleeding during pregnancy are the same as the patient's regular menses and the patient's history is accurate, this bleeding may be confused with a true menstrual period. The last regular period then cannot be determined with accuracy. In such cases, the date of the last menses cannot be used in a law court to determine the duration of pregnancy.

J. P. GREENHILL.

Martines: On the Histology of Cervical Polypi in Pregnancy. Folia gynaec. 26: 4, 1929.

Examining some polypi in the cervical canal of a woman, pregnant seven months, the author found the usual characteristics of this growth associated with abundant decidual reaction, surrounding the polypoid growths like a cuff. He thinks that the decidual elements originate from the investment cells of glands inclosed in the polypi, and therefore, these findings give support to Sfameni, who believes the placenta to be of an epithelial origin.

SYDNEY S. SCHOCHET.
JULIUS E. LACKNER.

Henkel: Abdominal Aspiration of Hydramnion Fluid. Deutsche med. Wehnschr. 56: 1249, 1930.

Abdominal aspiration for the relief of pregnant women suffering from pressure symptoms of a hydramnion is recommended in preference to perforation of the membranes by the vaginal route. The possibility of controlling the quantity of the drained fluid permits correction of fetal position and prevents the disastrous, premature separation of the placenta.

G. E. GRUENFELD.

Momigliano: On the Rôle of the Amniotic Epithelium in the Genesis of Hydramnios. Arch. di obst. & ginec. 16: 443, 1929.

From an examination of the structure of the amniotic epithelium in 11 cases of hydramnios, the author suggests that this epithelium participates in the genesis of hydramnios through a marked increase of the secreting surface.

SYDNEY S. SCHOCHET.
JULIUS E. LACKNER.

Kermauner: Constitution in Obstetrics. Wien. klin. Wchnschr. 43: 14, 1930.

The classification of individuals in terms of specific constitutional features and factors is not an acceptable procedure. The factors governing "constitution" are not constant being subject to change, and the period of change cannot be prophesied. Also, specific diseases may have definite and lasting effects which can bear no relationship to constitutional type. Very often the "constitution" of the individual is blamed for symptoms attributable to a large variety of overlooked conditions.

The inclusion of static-dynamic concepts such as irritability and resistance in the term constitution is of little practical value. In the last analysis each individual must be judged by himself.

In obstetrics "constitution" as an influence in the determination of results is found especially wanting. In the light of advances in the field of metabolism during pregnancy which were presented at recent gynecologic conferences and will take years to digest, constitution must be pushed farther and farther into the background. Constitutional factors have not been found to stand in direct relation to such conditions as hyperemesis gravidarum, thrombosis and embolism, chloasma and viteligo, and marked hirsuties. As far as relations to labor, labor pains, and postpartum hemorrhage are concerned the term only serves to cloak our ignorance. The same applies to considerations of multiple pregnancies and such conditions as the preponderance of males over females in any family.

FRANK SPIELMAN.

Arbruzzese: Relations of Constitutional Affinity of Parents to Fetal Development. Riv. ital. ginec. 11: 4, 1930.

Researches lead the author to the conclusion that fetal development depends upon the constitutional affinity or disaffinity of the parents. When parents are constitutionally different, more deficient fetuses are born, while in the case of parental similarity the fetus more likely is normal or overdeveloped.

SYDNEY S. SCHOCHET.
JULIUS E. LACKNER.

Jerlov, E.: The Lack of Hemoglobin During Pregnancy and a Suggestion on the Prophylaxis of Anemia. Acta obst. et gynec. Scandinav. 8: 356, 1929.

The author made hemoglobin determinations on 1143 pregnant women and found that 25.9 per cent of them had a hemoglobin of less than 70 per cent. He found a progressive decrease in hemoglobin as pregnancy advances. From the third month to the tenth, the average hemoglobin reading for each month was as follows: 83 per cent, 78.4 per cent, 78 per cent, 75.3 per cent, 75 per cent, 73.9 per cent, 73.2 per cent, and 71.1 per cent. Treatment by means of iron, arsenic and fresh vegetables produced an improvement in 90 per cent of the cases. In 5 per cent no change was observed and in the remaining 5 per cent the hemoglobin reading decreased in spite of treatment.

J. P. GREENHILL.

Suwa, Y.: Hematologic Investigation of Anemia in Pregnancy. Part I. Changes in the Blood Picture in Cases of Normal Pregnancy, Labor and the Puerperium. Japanese J. Obst. & Gynec. 13: 73, 1930.

The author examined the blood of 146 pregnant women. He found no change up to the fourth month either in primiparas or multiparas. However, in the middle of gestation there was a diminution in both the number of red blood cells and in the hemoglobin. In primiparas the greatest decrease was in the ninth month and in multiparas this occurred in the tenth month. A slight decrease was noted in the first and second stages of labor but the greatest drop occurred during the first to the third days after delivery. After that there was a gradual return to normal. As pregnancy advanced the number of leucocytes increased but during the eighth month they decreased. The number decreased during the puerperium, returning to normal between the fourth and seventh days.

J. P. GREENHILL.

Suwa, Y.: Hematologic Investigation of Anemia in Pregnancy. Part II. Anemic Women in Pregnancy, Labor and the Puerperium. Japanese J. Obst. & Gynec. 13: 79, 1930.

In a series of cases of anemia which occurred during pregnancy Suwa found the following causes for the anemia: (1) Chlorosis. This was more frequent in women between twenty and thirty-five years of age. It did not cause any complications during pregnancy but it was aggravated by the gestation. (2) Repeated hemorrhages during pregnancy. (3) Unexplained anemia during normal pregnancy. (4) Acute anemia due to hemorrhages during labor. (5) Pernicious-like anemia which is due to a toxemia of pregnancy.

J. P. GREENHILL.

Maisel, E.: Pernicious Types of Pregnancy Anemias. Zentralbl. f. Gynäk. 54: 2409, 1930.

True anemias of pregnancy recover spontaneously after delivery and in this respect are different from a pernicious anemia of the Addison, Biermer type. They occur usually in the second half of pregnancy and seem to have a predilection for parous women. The author's conclusions are: The pregnancy is the cause of the anemia; the children are premature and delicate; the birth is not attended with unusual bleeding; arsenic and iron are useful remedies, but the best treatment is fractional blood transfusion, 20 to 30 c.c. given daily or every other day on 7-10 occasions. Calf's liver, 100 to 150 gm. per day, is also very helpful.

WILLIAM F. MENGERT.

Item

The American Board of Obstetrics and Gynecology

The next written examination of the Board will be held in nineteen (19) different cities of the United States and Canada at 2 p.m. on Saturday, March 26, 1932. The general, oral and clinical, examination will be held in New Orleans on Tuesday, May 10, 1932, immediately preceding the meeting of the American Medical Association. Reduced railroad fares will be available. For detailed information and application blanks apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh, Pennsylvania.